INDEX

1922

EUGENICS LABORATORY PUBLICATIONS.

UNIVERSITY OF LONDON
FRANCIS GALTON LABORATORY FOR NATIONAL EUGENICS

THE TREASURY OF HUMAN INHERITANCE

EDITED BY KARL PEARSON, F.R.S.

VOLUME II

NETTLESHIP MEMORIAL VOLUME

BY

JULIA BELL, M.A., M.R.C.P.

CAMBRID
AT THE UNIVERSI
1933

PRINTED IN GREAT BRITAIN

PREFATORY NOTE

THIS volume, the second of the *Treasury of Human Inheritance*, was designed as a memorial to my friend and co-worker Edward Nettleship. No more enthusiastic believer in the importance of hereditary studies than Nettleship has ever arisen among our English ophthalmologists. The movement largely set going by him has borne good fruit, and will bear still more as the years go by. Sight is, perhaps, our most valuable possession both individually and racially, and a study of the material contained in this volume will undoubtedly enable its readers to appreciate how much remains to be done if we are to limit the spread of painful individual inefficiency and to check national ophthalmic degeneracy. Prevention is often feasible, but cure is nearly always doubtful, and not infrequently impossible.

In carrying out the design of the Nettleship volume I was indeed fortunate since I succeeded in enlisting the services of such a thorough and energetic inquirer as Dr J. Bell. The many years of laborious research involved in the preparation of this work mark a very noteworthy achievement. *Exitus acta probat.*

K. P.

April 30, 1933.

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UNIVERSITY OF LONDON
FRANCIS GALTON LABORATORY FOR NATIONAL EUGENICS

EUGENICS LABORATORY MEMOIRS. XXI

THE TREASURY OF HUMAN INHERITANCE

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VOLUME II

ANOMALIES AND DISEASES OF THE EYE

NETTLESHIP MEMORIAL VOLUME

PART I

RETINITIS PIGMENTOSA AND ALLIED DISEASES
CONGENITAL STATIONARY NIGHT-BLINDNESS
GLIOMA RETINAE

BY

JULIA BELL, M.A., M.R.C.S., L.R.C.P.

WITH PLATES I—XXVI FRONTISPIECE α AND COLOUR PLATE β
PEDIGREES 1—366

WITH A MEMOIR OF EDWARD NETTLESHIP

BY

J. B. LAWFORD, LL.D., F.R.C.S.

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And as Jesus passed by, he saw a man which was blind from his birth. And his disciples asked him, saying, Master, who did sin, this man, or his parents, that he was born blind? *St John*, IX. 1, 2.

ἄρχεται δὲ ὥσπερ καὶ τἆλλα νουσήματα κατὰ γένος. εἰ γὰρ ἐκ τοῦ φλεγματώδεος φλεγματώδης, καὶ ἐκ χολώδεος χολώδης γίνεται, καὶ ἐκ φθινώδεος φθινώδης, καὶ ἐκ σπληνώδεος σπληνώδης, τί κωλύει ὅτου πατὴρ καὶ μήτηρ εἴχετο τούτῳ τῷ νοσήματι, τούτῳ καὶ τῶν ἐγγόνων ἔχεσθαι τινά; HIPPOCRATES.

PRINTED IN GREAT BRITAIN

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SECTION VI

GLIOMA RETINAE

PREFATORY NOTE

THE publication of the pedigrees of hereditary eye diseases and anomalies was planned in 1911, but owing to the War the issue of the *Treasury of Human Inheritance* had to be suspended entirely, and now that the work is taken up again the difficulties are far greater than in 1911. In a labour of this kind there are two primary factors, the provision of highly trained research workers and the publication of their researches when they have been completed. The War left the Galton Laboratory in a precarious condition with regard to funds both for payment of research workers and above all for publication expenses. Owing to assistance granted during the last two years by the Medical Research Committee it has been possible for Dr Julia Bell to continue collecting data for the section of the *Treasury* dealing with eye diseases and anomalies. We have to record our gratitude to the Medical Research Committee for the aid provided, and to express a hope that the work as completed will be considered to have justified their support.

The death at a comparatively early age of Edward Nettleship was a severe blow not only to his personal friends but to all workers in the Eugenics and Biometric Laboratories. After retiring from private practice his aid had been most invaluable to us. His friendly help and sympathy could always be reckoned upon, especially in investigations that required accurate and cautious "field work" in the pursuit of hereditary characters, and none knew better than his colleagues in the preparation of the *Monograph on Albinism* issued by the Biometric Laboratory, how keen, suggestive and helpful Nettleship always was: we realised early in our relationship the extreme and unabating activity he would devote to the discovery of missing members of a pedigree, or to the recording of the exact nature of the disease or anomaly in individual cases. He was a born genealogist in the scientific sense, wherein genealogy means a record of characters rather than an index of names.

The one branch of medical science wherein the importance of hereditary studies has been fully appreciated and wherein splendid work has been done during the last decade is undoubtedly ophthalmology, and none can hesitate to admit that the main incentive towards this great achievement was the inspiration provided by Nettleship.

The loss of that inspiration was a great blow to those who were studying heredity with a view to its bearing on human progress. At first it appeared irreparable, and the only way to carry on the tradition seemed to be to show the full force of Nettleship's revelations by publishing a complete edition of his papers. But as the years went by this seemed less and less possible, and to some extent less necessary. For it became clear that Nettleship had created a school of ophthalmological geneticists and that his work would go on without such a stimulant. It then occurred to the Editor of the

Treasury that the best way to honour Nettleship's memory was to issue a volume of the *Treasury* devoted not only, as it must be, to Nettleship's own work and to that of his immediate students and friends, but to the work of all ophthalmologists who had contributed to our knowledge of hereditary diseases and anomalies of the eye. He felt sure from what he knew of Edward Nettleship during their conjoint work on Albinism, that he would much have preferred a *thesaurus* of all men's work to a special emphasis of his own contributions. The fitting memorial therefore seemed to be a comprehensive volume on the hereditary diseases and anomalies of the eye; and in that sense this section of the *Treasury of Human Inheritance* is issued as the Nettleship Memorial Volume. In this way the monument to Nettleship's inspiration and research will reach a wider audience and be of a more permanent character, for it shows not alone what Nettleship did but what he inspired other men to do as well.

While the field of this memorial volume has been thus extended, it is only fitting that it should contain some account of Nettleship's work and personality. Unfortunately the writer of this prefatory note could only speak of Nettleship after he had retired from active practice—of his enthusiasm, of his perseverance and of his suggestiveness in those days he can speak authoritatively—but he felt that more was needed than this, and it was with great gratitude and pleasure that he found Dr J. B. Lawford willing to supply an account of Nettleship's life and work. The volume when completed will also conclude with a bibliography of those papers of Nettleship which do not deal directly with heredity and accordingly are not included in the bibliographies of the separate sections of this volume.

We have most gratefully to acknowledge permission to reproduce pedigrees occurring in the *Transactions of the Ophthalmological Society of the United Kingdom*, the *British Journal of Ophthalmology*, the *Royal London Ophthalmic Hospital Reports*, the *Ophthalmic Review*, etc., from the various authorities concerned. In every case the original source is stated and the reader can easily refer to the fuller material there provided.

Of those who have aided with advice in the preparation of this work the Editor has to thank especially Mr C. H. Usher, who has always been most helpful when difficulties have arisen, and has given assistance of a most varied character in a number of important points. Professor W. Bulloch also kindly consented to read the introductory matter and made valuable suggestions for its improvement.

Lastly the long-standing indebtedness of the Galton Laboratory to Miss H. Gertrude Jones has been still further increased by the arduous task she voluntarily undertook of drawing the whole of the twenty-six plates of this instalment of the *Treasury*. This is a contribution to the success of the volume that only those who are familiar with much of the published pedigree work will fully appreciate. One of the chief difficulties in a volume of this kind is to ensure accuracy and clearness in the pedigree plates, and we are confident that the maximum of what is possible in this direction has been achieved in the original beautiful drawings of Miss Jones.

One last word to the numerous subscribers and other friends of the pre-war *Treasury* must be spoken here. The Editor has waited and hoped in vain for a substantial fall

in the post-war cost of publishing a work of this kind. The cost is practically three times what it was when we started the *Treasury*, and although it seems impossible to hope that the work will ever pay its way, it has been absolutely necessary to raise the price of issue to such an amount that the loss is not prohibitive of any further publication at all.

Several other sections of the work are in progress and the rapidity of their issue entirely depends on the sympathy this resumption of publication meets with.

K. P.

The Galton Laboratory,
University of London.
September 4, 1922.

I believe when the truth of heredity as respects man shall have become firmly established and be clearly understood, that instead of a sluggish regard being shown towards a practical application of this knowledge, it is much more likely that a perfect enthusiasm for improving the race will develop itself among the educated classes.

FRANCIS GALTON.

EDWARD NETTLESHIP, F.R.S., F.R.C.S. 1845—1913

By J. B. Lawford, LL.D., F.R.C.S.

Edward Nettleship, born at Kettering, Northamptonshire, was the fourth son of Henry John Nettleship, solicitor, of that town. His mother was Isabella, daughter of the Rev. James Hogg, Rector of Geddington, and sometime Head Master of Kettering Grammar School. His paternal ancestry has been traced through six generations to one John Nettleship, of Bole, Notts, whose will was proved in 1730/1. John had two sons by his first wife, from one of whom, Richard, is descended the line which so far as sons are concerned has been terminated recently by the death of the only survivor of Edward Nettleship's sibship. John and his son Richard lived at Bole, but the succeeding four generations were resident in Gainsborough, where Henry John Nettleship, Edward's father (the eldest of a large family) was born in 1807. The house of Edward's grandfather in Gainsborough, where his widow and her five daughters were living, is referred to in Vol. I of Mozley's *Reminiscences of Towns, Villages and Schools* as "A Sunlit Spot," and the mother and daughters are described in eulogistic terms. Edward Nettleship was one of seven children, six of whom were boys. The only girl died in early infancy and the youngest boy died at the age of fifteen. Of the five brothers who grew to manhood, four, including the subject of this memoir, became distinguished in their several professions. The eldest, Henry Nettleship, held the Corpus Professorship of Latin, at Oxford, for fifteen years, and was a man of high attainments and wide interests. The second son, John Trivett Nettleship, achieved reputation as an animal painter, and as the author of the first serious study of Browning's poetry. The fifth son, Richard Lewis Nettleship, Fellow and Tutor of Balliol College, Oxford, was a man of remarkable personality and unusual gifts; his untimely death in 1892, from exposure in the Alps, cut short a career of great promise. All three died before their brother Edward.

Henry John Nettleship (Edward's father), described as rather shy and reserved in character, was a man of considerable intellectual power, with a developed taste for poetry and music; both these traits were manifest in varying degrees in his sons, especially in the eldest who was an accomplished pianist. His wife, who at her death at Oxford, at the age of 81, was alluded to as the "mother of the Nettleships" was a woman of strong character, and although physically an invalid her will dominated the household. She was a firm believer in strenuous intellectual exercise, which she preached and practised in the training of her sons: her strongly marked asceticism led to her sons being debarred from all forms of social frivolity and even from many outdoor games during their boyhood, though they were permitted, and had facilities for, such amusements as riding. Edward Nettleship received his early education as a day boy at Kettering Grammar School. His three elder brothers had obtained scholarships at

their respective public schools, but his parents considered that Edward was better suited for studies other than classics or mathematics. The Head Master of the Grammar School at that time, Mr Turle, was an enthusiast in natural history, and imparted his enthusiasm to his pupil who had already manifested a liking for such pursuits. One result of this was that the lad led rather a solitary life out of school, spending his Saturdays and half-holidays in exploring the woods near his home, becoming familiar with the habits of birds and other woodland creatures. Geddington Chase, near Kettering, was a paradise for the young naturalist and the head keeper, whose cottage was in the midst of the wood, was a firm friend and ally and gave him welcome assistance in his search for birds' nests and other objects of interest. Cranford Rectory, near Kettering, which had a large half-wild garden was also a favourite haunt. The boy's love of outdoor pursuits led to the decision that he should become a farmer, and after leaving the Grammar School in 1861 he spent some months on a farm at Kimbolton. Thence he went to the Royal Agricultural College at Cirencester. His record for the next few years is one of extraordinary activity and the accomplishment of a prodigious amount of study. In 1863 he became a member of the Royal Agricultural College. He then entered as a student at the Royal Veterinary College, Camden Town, and at King's College, London; and in 1867 obtained the diploma of Licentiate of the Society of Apothecaries. In the same year he became a member of the Royal College of Veterinary Surgeons, and shortly afterwards was appointed professor of Veterinary Surgery at the Cirencester College, in succession to Mr William Hunting, but did not retain this post for more than a year. In 1868 he obtained the membership and in 1870 the fellowship of the Royal College of Surgeons. Shortly before this he had joined the London Hospital where he became a dresser and at a later date assistant to Sir (then Mr) Jonathan Hutchinson. This was the beginning of a long and intimate friendship which was terminated only by Hutchinson's death not many months before that of his former pupil.

In 1867 or 1868 Nettleship began to give special attention to ophthalmology. He entered as a student at Moorfields Eye Hospital, becoming one of Hutchinson's clinical assistants and an associate and close friend of Waren Tay, acting in the same capacity. In later years Nettleship and he were colleagues on the staff of the hospital. In May 1871 Nettleship was appointed curator of the museum and librarian to the hospital and held this post for $2\frac{1}{4}$ years. Ocular pathology was then in a comparatively early stage and the large amount of material at Moorfields afforded abundant scope for investigation. Nettleship made good use of his opportunities and published several papers of importance. The "Curator's Report" in Vol. III of the *Ophthalmic Hospital Reports* appears to be the earliest of his writings upon ophthalmic subjects. In 1873 he was appointed medical superintendent of the Ophthalmic School at Bow opened by the Local Government Board, in an unused workhouse, for the reception and treatment of cases of ophthalmia and other chronic diseases, drafted from the West Surrey District Schools at Anerley: this was a very difficult post and only his tact and organising power enabled him to fill it successfully. A year later he was asked by the L. G. B. to inspect and report upon the Metropolitan Poor Law Schools in

reference especially to the prevalence of ophthalmia and the measures for dealing with it. This report was published in 1874 and led to some much-needed reforms in the care of pauper children. About the same time he wrote a long and valuable paper embodying the results of his investigations concerning Granular Conjunctivitis, which was published in the *British and Foreign Med.-Chir. Review* for 1874–75.

Nettleship's first appointment on the staff of a hospital was at the South London Ophthalmic Hospital (now the Royal Eye Hospital). He resigned this post in 1878, when he was elected ophthalmic surgeon to St Thomas's Hospital and lecturer on ophthalmology in its medical school, in succession to R. Liebreich. The latter, appointed ophthalmic surgeon to St Thomas's when the new buildings on the Thames Embankment were opened in 1871, was the first specialist in charge of the eye department. During his tenure of office the clinic increased rapidly and was attended by a large number of patients. Under Nettleship's *régime* it became more widely known and by his efforts was brought to a degree of perfection previously unequalled in this country. Nettleship remained on the staff of the hospital until 1895. His work there was carried out with conspicuous ability and his reputation as an ophthalmic surgeon and as a teacher became firmly established. His merits and business capacity were so highly esteemed by his colleagues that in 1888 he was asked to accept the position of dean of the medical school at a somewhat critical period in its history. Although an exceptionally busy man, he undertook the heavy additional duties which this office entailed and carried them out with his usual thoroughness for three years. His name and reputation are still cherished and honoured by those who were associated with him in the hospital and school either as colleagues or pupils.

The next important incident in Nettleship's professional career, and one peculiarly gratifying to him, was his election as assistant surgeon to Moorfields Eye Hospital in 1882. His was the last election to the staff of that hospital conducted on the old plan, whereby every governor of the hospital (there were several hundreds) had to be provided with a copy of the candidate's application and testimonials. The writer of these lines remembers very well assisting Nettleship in this onerous task. Five years later Nettleship became surgeon to the hospital and remained on the active staff until 1898. On his retirement he presented a considerable sum of money to the committee of the hospital to be expended in the purchase of instruments or apparatus for pathological or physiological investigation. Other hospital appointments held by Nettleship, though for comparatively brief periods, were those of ophthalmic surgeon to the Hospital for Sick Children, Great Ormond Street, and assistant surgeon to the Hospital for Skin Diseases, Blackfriars.

Early in 1880 a number of surgeons and physicians interested in ophthalmology decided to found a society for the advancement of this branch of medical science, and the Ophthalmological Society of the United Kingdom came into being, with Mr (subsequently Sir) William Bowman as its first president. Nettleship took a prominent part in the preliminary arrangements and became the first surgical secretary, his medical colleague being Dr (afterwards Sir) Stephen Mackenzie. From the outset Nettleship took a keen and active interest in the society and never relaxed his efforts to further

century. This association encouraged and abetted his zeal in the investigation of disease, and probably confirmed his habit of note-taking of which Hutchinson was a past master. To the end of his professional career Nettleship took abundant notes of every case of interest or importance which came under his observation, notes which, as the writer knows well, are models for any medical man.

Although Nettleship's reputation as a surgeon and a scientist is permanently established, his place in the memory of many men was gained by his ability and attractiveness as a teacher. As a lecturer in a class-room or theatre he was not at his best; he was not eloquent and his voice was not sufficiently powerful; as a clinical teacher of the individual, or of a group of students, he had few equals; he excelled especially in post-graduate teaching. During the active period of his service at Moorfields Hospital, his qualities as a teacher became widely recognised; these added to his magnetic personality attracted many of the best students to his side, most or all of whom soon became imbued with his spirit and with his assiduity in the investigation of disease, and were infected by his enthusiasm. He did not suffer fools gladly and had no use for the man whose clinical work was slovenly or inaccurate. Ignorance, provided the desire for knowledge was evident, was no bar, and no genuine seeker ever failed to obtain his help. Few if any of those who worked with him at St Thomas's or Moorfields will ever forget the splendid example in the methods of clinical enquiry set by their teacher.

In practice Nettleship gained and retained the confidence and loyalty of his patients to a remarkable degree. He was far from being all things to all men, but his obvious sincerity and straightforwardness, and his genuine kindness and sympathy were quickly recognised by the large majority. The writer has had many opportunities of learning from former patients how greatly they valued his advice and friendship.

In Nettleship's personal character there was much that was noteworthy and much that called forth admiration. Broad-minded and well-informed he possessed to an unusual degree the judicial mind, and his judgment in complex questions was seldom at fault; high ideals, scrupulous integrity and hatred of everything false or untrue were prominent traits. His natural reserve masked in some degree his decision of character, his determination and his unbounded energy.

Throughout his life Nettleship was an indefatigable and tireless worker, and accomplished a great deal while others slept, his habit being to rise very early and work when all was quiet. To those who gained his confidence he was a staunch and loyal friend, and many of his acts of kindness were known only to the recipients. He exerted a remarkable and far-reaching influence for good on many who were brought into contact with him, both young and old, and had no more devoted admirers than children and young persons. Some of these now well advanced in years have expressed in grateful terms their indebtedness to Nettleship's example and precept. The writer, who had the privilege of a long and close association with Nettleship, has had for many years an unbounded admiration for the true nobility of his character and a deep appreciation of his warm-hearted and sympathetic nature. These qualities were, naturally, even more fully realised by those in his immediate circle; of this there has been abundant testimony in letters from relatives and intimate friends. In 1869, before his medical

studies were completed, Nettleship married Elizabeth Endacott, daughter of Mr Richard Whiteway, of Compton, Devon; they lived at first in Grafton Street in furnished rooms: subsequently for a period of eighteen months, they shared a house in Finsbury Pavement with his friend and colleague, Mr Waren Tay, and then, in order to be near the London and Moorfields Hospitals, they took "a little old-fashioned creeper-clad house with a garden" at Stepney, where they had two students living with them. Their stay in this pleasant abode was followed by a dreary year of residence in the Bow Ophthalmic School referred to above, after which they moved to Wimpole Street.

When visiting the Hutchinsons at Haslemere, the beauty of that part of Surrey captivated Nettleship and his wife, and in 1885 he bought land at Hindhead on which he built a charming house, completed in 1887. Here, whenever his work permitted, Nettleship spent many happy days, working in the garden and the woods which were to him a constant source of delight. His love of country life, birds, trees and flowers, grew with advancing years and probably he was never happier than at Hindhead. Many of his friends retain most pleasant memories of the kindness and hospitality of himself and Mrs Nettleship in their Surrey home. In 1910 they moved to a smaller house pleasantly situated on the side of a hill with a beautiful outlook across a valley. In this house, surrounded by the trees and flowers he loved, Nettleship died; and here his widow still resides.

This sketch would be very incomplete without a brief reference to Nettleship's partner in life, one who cheerfully shared the struggles of his early days, and rejoiced in his well-deserved success. Few men have had so loyal and devoted a helpmeet, and it is easy to imagine how greatly the companionship of one so gifted with womanly charm and true sympathy helped to smooth the rough places on life's pathway.

SECTION I

RETINITIS PIGMENTOSA AND ALLIED DISEASES

CHAPTER I

GENERAL ACCOUNT

This title must inevitably recall the name of Nettleship to all interested in the inheritance of eye disease, it was taken from his writings, and was indeed chosen in order to emphasise his pioneer work on the subject and the stimulus which he provided to the younger ophthalmologists of his day to work in the same field. We have again, with Nettleship, included as diseases allied to retinitis pigmentosa, retinitis pigmentosa sine pigmento, retinitis punctata albescens, gyrate atrophy of the choroid and retina, choroideremia, and the two distinct types of congenital stationary night-blindness.

Nettleship included choroideremia in his group for clinical reasons believing it to be improbable that this condition, which he described as 'developmental rather than pathological,' bore any relation to retinitis pigmentosa, but the extraordinarily interesting pedigree published by Smith and Usher (see Fig. 119) showing choroideremia in a boy whose mother and one sister had retinitis pigmentosa and whose father had congenital stationary night-blindness, definitely links it up with one or other of these conditions and Zorn's pedigree (see Fig. 262) showing its occurrence in the same family with atypical retinitis pigmentosa and possibly gyrate atrophy of the choroid and retina suggests that choroideremia is in fact allied to retinitis pigmentosa, and we happily do not longer need to make any apology for including it under our title; indeed it is now well recognised that retinitis pigmentosa itself is a developmental defect, the exact nature of which is still obscure. For congenital stationary night-blindness the case is different; both types of this condition are undoubtedly due to some developmental defect but nothing is known of the nature of the defect and we have no reason other than convenience for placing either type of the condition under our title, the common symptom of night-blindness being the only link between this disease and retinitis pigmentosa, and this symptom though very usual in the latter disease is by no means invariably present.

It is greatly to be regretted that we still as in Nettleship's day have to admit a complete ignorance of the pathology of congenital stationary night-blindness, no *post-mortem* examination having yet been made on the eye of any person suffering from it; this omission is explained by the rarity of the condition and by the fact that it never leads to a need for excision of the eyeball during life; but such ignorance should not be for ever insurmountable.

(α) *Historical.* It is evident that before the invention of the ophthalmoscope we could expect to find no differentiation of the various conditions included under our title, unless it were to distinguish between retinitis pigmentosa, characterised by its

progressive nature leading to blindness and by its contracted fields of vision even in bright daylight in advanced cases, as opposed to the stationary night-blindness associated with no disability of vision by day; but congenital stationary night-blindness is a very rare condition now and we have no evidence that it has ever been less rare, and it may easily have escaped detection as a clinical entity in the days when there were only very few writers on ophthalmology; it is perhaps more remarkable that retinitis pigmentosa, with its frequent hereditary nature, its train of symptoms and the very characteristic attitude of its victim who ultimately has only direct vision and peers round to look at everything as a result of his contracted fields, should have escaped recognition as an entity by, say, such an astute observer as Hippocrates. A careful search through the works of a large number of early writers has failed to reveal anything more suggestive of the existence of retinitis pigmentosa or stationary night-blindness in their days than the statement made by some of them in discussing the symptom of night-blindness that occasionally the condition has not responded to treatment, or has progressed to complete loss of sight.

It may be well here to consider for a moment the symptom of night-blindness which has been variously described as nyctalopia, lusciosus, hemeralopia, dysopia tenebrarum, amblyopia crepuscularis, as moon-blindness by sailors from the belief that it was produced by the action of moon-beams falling on the eyes of those who were exposed to them during sleep, and finally as hen-blindness from the fact that hens were believed to be normally night-blind and to go to roost when the sun sets because they could no longer see to pick up grains of wheat. There has been much discussion and controversy as to whether or no Hippocrates and other early writers used the word 'nyctalopia' in the sense of night-blindness or day-blindness and the doubt has led to much confusion. The point was discussed exhaustively by Greenhill (see Bibl. 109) and by Tweedy (see Bibl. 116) and the general opinion is in favour of night-blindness as the correct translation, though the cautious reader would hesitate to pledge himself to a diagnosis of the condition described by Hippocrates in the following words—"Nyctalopia is most apt to attack young persons, either males or females, and to pass off spontaneously on the fortieth day or in seven months, and in some cases it endures for a whole year. Its duration may be estimated from the strength of the disease and the age of the patient. They are relieved by deposits which determine downwards, but these rarely occur in youth. Married women and virgins that have the menstrual discharge regular are not subject to the complaint. Persons having protracted defluxions of tears who are attacked with nyctalopia, are to be questioned whether they had any previous complaint in the head[1]."

However this may be, the symptom of night-blindness has been recognised and described by writers of all ages in all countries but in most cases temporary night-blindness only was referred to even as late as the nineteenth century; it has been noted in association with malnutrition, nerve exhaustion, xerosis conjunctivae, choroiditis syphilitica, rheumatism, lead colic, hysteria, scurvy, onanism, pregnancy, ergo-

[1] The genuine works of Hippocrates, translated by Francis Adams, London 1849, *Appendix to The Book of Prognostics*. Vol. I., p. 267.

tism, cholera, helminthiasis, malaria, disorders of the stomach, liver or kidney disease, with "weakness in the head and especially a thickening of the optical pneuma and of the other humours and membranes of the eye," it has also been described as a result of living in marshy places and was noted in certain cases of ague in the Lincolnshire fens, finally it has been noted as a result of dazzling. In all cases the cure for night-blindness prescribed with extraordinary persistence throughout the ages all over the globe has been very much as follows—"Nyctalopic persons should be treated, if robust, with venesection at the elbow and at the corners of the eyes, but when the humours are corrupt, by purification with a proper purgative. Then, after the general evacuation of the body, gargles should be employed and purification should be practised through the nose and sneezing excited..... Goats'[1] liver appears to be of use to these patients with salt but roasted without oil and eaten very hot. Others however are accustomed to anoint the eye with the broth which exudes from the liver during the roasting; others during the roasting have the eyes held open in the uprising steam and so foment them.....[2]." This last prescription of liver for night-blindness is of great antiquity[3], and appears to date as far back as the famous 'Book of the Eyes' in the Egyptian Papyrus of 1500 B.C. found between the bones of a mummy in the Theban Necropolis, which came into the hands of Ebers in 1872 and was deciphered by him; in this work the roasted liver of an ox is prescribed for some unnamed disease of the eyes and this treatment has been thought to suggest that the unnamed disease was night-blindness and that thus this disability was recognised in Egypt some 3400 years ago. Guthrie in 1794 gives an interesting account of epidemic "hen-blindness" in Russia following the lenten fasts and of its rapid cure by means of an infusion of *centaurea cyanus* (corn flower); he refers to it as a curious disease of Russia which he never remembers to have been treated by any British physician[4]. Bampfield writing in 1814 described night-blindness associated with scurvy in sailors which he proceeded to cure by means of blisters[5].

A great number of similar references might be given and if we search amongst them for signs of a failure to cure, and thus for possibly early references to retinitis pigmentosa though unrecognised as such by the writers, we find a condition described by Bontius[6] in 1642 which may or may not have been night-blindness but has been frequently cited as such; to quote from a translation of his work by a Physician in 1769 "The people who sail to Amboyna and the Molucca Islands are often troubled with a weakness of sight and even a total blindness arising from thick and viscid humours stuffing the head and brain and obstructing the optic nerves: which blindness,

[1] The liver of a goat was prescribed from the belief, as Pliny reports, that this animal sees by night as well as by day. See Bibl. No. 2.

[2] Taken from Aëtius of Amida who lived 502—574 A.D. Translated by Shastid in article on "The History of Ophthalmology" in *The American Encyclopedia of Ophthalmology*, Vol. XI., pp. 8664—65, Chicago 1917. For early reference see Bibl. No. 4.

[3] And has survived the ages, for cod liver oil, or even liver to be eaten are still prescribed in certain cases of night-blindness though we no longer specify that the liver should be from a *he*-goat or from a black cock, or black swine, etc.

[4] Bibl. No. 22. [5] Bibl. No. 23. [6] Bibl. No. 13.

however, is not perpetual but often ceases upon a change either of air or better diet. The inhabitants of these islands impute it to eating hot rice." Bontius then proceeds to describe how he cures the condition by purges, sternutatories, masticatories and bleedings, and adds that the grand specific in this disorder is our old friend the liver, this time, of the fish *Lamia* eaten crude with salt; he says finally—"upon the whole though this blindness is often transitory yet if neglected and an improper diet be persisted in with an unseasonable use of arrac, it often degenerates into a total deprivation of sight of which everywhere here we meet with instances." Etmuller[1] in 1701 writes "Nyctalopia si interdiu recte, vesperi parum aut nihil videtur, raro curatur." Maitrejean[2] in 1707 refers to the night-blindness which can be cured and the night-blindness which cannot be cured and infers that it is only possible to determine which case is being dealt with by watching the effects of treatment. From this date onwards the knowledge that night-blindness cannot in all cases be cured and may under the most favourable conditions progress to complete blindness by day also, becomes more general, though as late as 1814 Bampfield is found to state that night-blindness only progresses to complete blindness as a result of a failure to receive proper treatment.

It may by no means be taken for granted that the condition of temporary night-blindness occurring with its varied associated diseases is totally without interest to us writing of retinitis pigmentosa and allied diseases; little is known of the mechanism of its production, indeed we do not even know whether it is of central or of peripheral origin. A great number of people live in low-lying unhealthy districts without becoming night-blind, and yet Zimmermann[3] in 1883 describes a family of four children living in such a district who all became night-blind and remained so until they moved to a healthy district when they all recovered; may there then be a family predisposition to develop temporary night-blindness under certain conditions? A case described by La Serre[4] in 1688 (see Plate XXII, Fig. 291) has been quoted as the earliest recorded case of inherited night-blindness; this was also a case of temporary but recurrent night-blindness which occurred every year towards the month of May and persisted for three or four months; a paternal aunt of the patient and two children of this aunt were affected in the same way.

It would be of interest to know whether normal members of stocks in which retinitis pigmentosa or congenital night-blindness occurs tend to become night-blind under conditions apparently favourable to its production more readily than do members of normal stocks. When we look for early references to the inheritance of permanent night-blindness the information is very scanty. The first definite record we have found is due to Ovelgün[5] as late as 1744 when he reports a history of night-blindness in a brother and sister and in the sons of two of their mother's paternal uncles (see Plate XXII, Fig. 292); he also gives some evidence to suggest that the case was one of retinitis pigmentosa. From this date we find no further reference until 1830 when Richter[6] describes congenital night-blindness in three members of a sibship of nine whose parents and other relatives were free from the defect (see Plate XXII, Fig. 297).

[1] Bibl. No. 16. [2] Bibl. No. 17. [3] Bibl. No. 127.
[4] Bibl. No. 18. [5] Bibl. No. 19. [6] Bibl. No. 24.

Eight years later we find the pioneer work of Cunier[1] describing the famous Nougaret family with its history of congenital stationary night-blindness in six generations. This pedigree was brought up to date and extended to ten generations in 1907 at the suggestion of Nettleship[2], who went over to Vendémian himself and examined certain members of the family with the ophthalmoscope for the first time, thus being able to pronounce the case to be one of congenital stationary night-blindness and not one of retinitis pigmentosa or any condition involving changes in the fundus (see Plate XXIV, fig. 317). Cunier's work must have appeared as a rather startling announcement to the ophthalmologist of his day, and it is surprising that it did not stimulate the immediate production of other family histories, but we find no further pedigree of the kind until nine years later when Stiévenart[3] in 1847 publishes an interesting history of congenital stationary night-blindness affecting both sexes, as in Cunier's case, and extending this time through four generations (see Plate XXIII, fig. 305). This was the last case of inherited night-blindness found in the literature before the invention of the ophthalmoscope, indeed so far were the authors of that day from a true recognition of the intensity of inheritance for these conditions that a writer whose works on surgery extended over four volumes was able to state—"...l'amaurose peut être congéniale; quelques observations, incomplètes à la vérité, porteraient à croire qu'elle est quelquefois héréditaire," or again "On trouve dans les Ephémérides des Curieux de la Nature, décade II. ann. 6, obs. 79[4], un fait qui porterait à croire que l'héméralopie est quelquefois héréditaire, si un seul fait suffisait pour prouver l'action d'une telle cause[5]."

And now we come to the invention of the ophthalmoscope in 1851, when pigmentation of the retina could first be seen in the living subject and it became possible to classify cases in which night-blindness was a symptom on the basis of the condition found on an examination of the fundus. Pigmentation of the retina had been described post mortem, under the name of 'melanosis retinae,' by Langenbeck[6] in 1836, and von Ammon[7] in 1838 gives a coloured illustration of the condition in his atlas; but there was at this time no recognition in the clinic of the correlation of pigmentation of the retina with the symptoms of what we now describe as retinitis pigmentosa. The acquisition of the ophthalmoscope completely revolutionised the work of the ophthalmologist and immeasurably widened his scope and knowledge, though it is sad to have to admit that, so far as our group of diseases is concerned, the benefit from the discovery was chiefly if not entirely limited to the ophthalmologist, and has contributed little or nothing to relieve the gloomy prospect for the patient to this day.

It becomes clear then that since cure is not to be expected prevention is the all-important problem and a knowledge of the etiology of the condition and numerous illustrations of its varied degree of inheritance become of great urgency.

It was perhaps the recognition, conscious or unconscious, of this position, stimulated doubtless by the beauty and interest of the picture revealed by the ophthalmoscope, which contributed to the production of what we might almost describe as an

[1] Bibl. Nos. 27, 28. [2] Bibl. No. 243. [3] Bibl. No. 30. [4] La Serre's case.

[5] Boyer, P. *Traité des maladies chirurgicales.* Paris 1847. T. IV., p. 602 and p. 616.

[6] Bibl. No. 25. [7] Bibl. No. 26.

epidemic of inaugural dissertations, theses or journalistic articles on retinitis pigmentosa in the latter half of the nineteenth century, some of which were excellent, some bad and others indifferent; the story was told and repeated and again repeated of how van Trigt[1] in 1853 first described the disease, in a case at the Donders clinic at Utrecht, as seen through the ophthalmoscope; how von Graefe[2] at about the same time described the disease in Berlin under the name of *morbus Arianus*, having observed it in a patient, the Spanish Marquis Ariani; of how Donders[3] first named the disease retinitis pigmentosa in 1857, a bad name suggesting that the disease is of inflammatory origin as indeed for many years it was believed to be. Again it is told and retold how Leber[4] first described *retinitis pigmentosa sine pigmento*; how Mooren[5] in 1882 first described and named *retinitis punctata albescens*; how Fuchs[6] in 1896 first described and named *atrophia gyrata chorioideae et retinae*; how Mauthner[7] in 1872 first described a case of choroideremia; and how Leber[8] as late as 1877 first described congenital stationary night-blindness. All writers at this period described cases and fully recognised the need to inquire into the family histories and to consider the question of associated diseases or defects; they provide much valuable information, often very scanty so far as individual cases are concerned but throwing much light on the significance of the various factors concerned, when all available material is collected and classified.

The need for collecting and classifying all available information was realised and carried out exhaustively by Nettleship[9], whose interest in the inheritance of eye disease was, we suspect, possibly stimulated originally by Jonathan Hutchinson: so thorough was the collection of data made by him in 1907—8 from which we take our title that we have been able to find extremely little of interest or significance, bearing on the subject and published before that date, which is not included either in his text or his bibliography; in addition to this Nettleship certainly contributed more fully worked out pedigrees from the patients who consulted him than any other writer up to his date.

And since the date of Nettleship? Well, the reader has only to glance for a moment at Plate VIII, Fig. 119 and at Plates IX—XVII, Figs. 133—173, in order to grasp something of the nature of the contribution of Usher[10], the pupil and friend of Nettleship, to our subject. Other recent contributions which appear to the writer to be of rather special interest are the lecture by Doyne[11] in 1910 emphasising some of the more obscure and less generally recognised signs and symptoms of retinitis pigmentosa; the extremely suggestive and perhaps revolutionary paper by Treacher Collins[12] on the etiology of retinitis pigmentosa published in 1919; the pedigree of congenital stationary night-blindness in an American family, published by Newman[13] in 1914; and the pedigree by Mücke[14] of retinitis pigmentosa which presents many points of interest.

[1] Bibl. No. 31. [2] Bibl. No. 47. [3] Bibl. No 36. [4] Bibl. No. 72.
[5] Bibl. No. 114, p. 217. [6] Bibl. No. 187. [7] Bibl. No. 78. [8] Bibl. No. 98.
[9] Bibl. No. 251. [10] Bibl. Nos. 301, 310. [11] Bibl. No. 268. [12] Bibl. No. 318.
[13] See Plate XXIV, fig. 321. Bibl. No. 300. [14] See Plate XIX, fig. 212. Bibl. No. 327.

(β) *Signs and Symptoms.* The three classical symptoms of retinitis pigmentosa, which are very generally described as diagnostic of the disease but are not invariably present, are night-blindness, contraction of visual fields and ophthalmoscopically visible pigmentation of the retina; other characteristics are the early, or in some cases congenital, onset of the disease and its slow maturity progressing to complete blindness in middle age but retaining relatively good central vision until an advanced stage of the disease; the disease is usually bilateral; signs of atrophy of the disc are usually present and narrowing of the retinal vessels, the larger of which may degenerate into mere threads and the smaller vessels may disappear altogether. Further, more obscure and less generally recognised symptoms of retinitis pigmentosa noted by Doyne[1] are as follows: i. the persistence of images; ii. in advanced cases there is often a marked preference of the patient for a particular degree of artificial light; iii. he describes a momentary sensation of bright light circling round the periphery of the visual field; iv. there is a zone of greyish infiltration situated immediately inside the main pigmented zone characteristic of the disease; v. a layer of fine opalescent vitreous opacities may almost always be detected lying immediately anterior to the retina.

To consider some of these symptoms in more detail. Night-blindness is perhaps the first symptom to appear and is very generally present, it is present however to a varying degree, every grade being described between the case of the patient who becomes absolutely blind in a dim light and the patient who does not know that he sees less well than other people in the dark and in whom the defect is only demonstrated on an estimation of the light sense by means of a photometer; or again this symptom may in rare cases be absent altogether. Thus Marlow[2] describes a case of retinitis pigmentosa with extreme contraction of the visual fields and without night-blindness; Axenfeld[3] reports several cases in which night-blindness was not complained of and in one case could not be detected by the use of a Förster's photometer; Hutchinson[4] describes a case of retinitis pigmentosa in an advanced stage which had been progressing during twenty years or more in which night-blindness was not present. Illustrations of cases in which night-blindness has not been demonstrated or is not of a marked order may be seen in the following pedigrees of our series: Plate II, Fig. 5; Plate V, Fig. 65; Plate VI, Fig. 89; Plate VII, Fig. 116; Plate VIII, Fig. 119; Plate X, Fig. 137; Plate XIII, Figs. 147, 150, 152; Plate XIV, Fig. 155; Plate XV, Fig. 160; Plate XVIII, Figs. 190, 199, 200; Plate XIX, Fig. 215; Plate XX, Fig. 249; and Plate XXII, Fig. 288[5].

The determination of the exact form of the visual fields in retinitis pigmentosa is of some difficulty owing to the varying results obtained at different times and under different conditions of lighting, and owing also to the fact that a certain amount depends upon the intelligence of the patient, but it is in the opinion of some clinicians of great diagnostic importance and aids in the differentiation of primary retinitis pigmentosa from that type of the disease which is secondary to a chronic disease of the choroid. Von Graefe[6] first drew attention to the fact that a greatly contracted visual field with relatively good central vision was a special feature of retinitis pigmentosa,

[1] Bibl. No. 268. [2] Bibl. No. 178. [3] Bibl. No. 257. [4] Bibl. No. 66.
[5] See *Description of Pedigree Plates*, p. 47 *et seq.* [6] Bibl. Nos. 35, 38.

he noted that the retraction might be excentric and that ring scotoma might be present. Gonin[1] after careful investigation concludes that the retraction of visual fields in this disease is not really concentric; that the first disturbance of vision takes place in an equatorial zone and spreads from there in a direction centrifugal and centripetal, and that the functions of the extreme periphery and of the macular region are maintained until a relatively late stage of the disease; he concludes further that in most cases the peripheral zone of vision is lost before the central field, also that the presence of a ring scotoma is the rule and not the exception as is maintained by some observers. Other interesting observations on the subject have been described by Hepburn[2] and by Usher[3]. Most authors merely describe a *concentric* contraction of fields but there has been, and indeed still appears to be, some difference of opinion on this point between authors who have done a considerable amount of work on the subject.

The ophthalmoscopic picture of pigmentation of the retina in typical cases is very characteristic. The visible deposits of pigment have migrated from the pigment epithelium into the internal layers of the retina; they collect chiefly along the vessels and may be found in their perivascular sheaths[4]; when the vessels branch a typical deposit is formed, which has been likened to a bone corpuscle, with fine processes which interlace to form a coarse network; deposits in the macular region change their character from the absence of vessels there and are seen merely as granules. In an early case pigment is seen characteristically in the equatorial zone only, but with the progress of the disease the distribution extends peripherally and centrally until the whole fundus may appear to be covered with a coarse black net. With the migration of pigment from the epithelial layer of the retina the choroidal vessels become visible and give a tesselated appearance to the fundus. The condition however presents every variety in intensity from a dense or diffuse distribution extending from the extreme periphery to the macula itself, to a total absence of pigment in the internal layers of the retina, and although pigmentation extending to the macula is perhaps always associated with extreme contraction of fields and severe visual defect, the converse is by no means the case, for cases are on record in which the fields are contracted to the fixation point with severe defects of central vision without a trace of pigment becoming visible. Such cases are known as *retinitis pigmentosa sine pigmento*. Cases are more frequently described in which no pigment is visible on a first examination but typical deposits are seen to appear at a later stage of the disease.

Pedigrees of our series in which cases occur showing little or no pigment relatively to the stage of the disease as indicated by other signs and symptoms may be seen as follows: Plate II, Figs. 7, 8, 9, 11, 12, 16; Plate III, Figs. 21, 25; Plate IV, Fig. 33; Plate VI, Fig. 72; Plate XI, Figs. 140, 142; Plate XIII, Fig. 150; Plate XIV, Fig. 158; Plate XVI, Fig. 166; Plate XVII, Figs. 175, 178, 179; Plate XIX, Figs. 212, 215, 217; Plate XX, Figs. 223, 227, 235, 239, 241, 242; Plate XXII, Fig. 294[5]. An examination

[1] Bibl. Nos. 215, 218, 222. [2] Bibl. No. 249. [3] Bibl. No. 301, pp. 137—145.

[4] Nettleship says "when visible vessels are ensheathed in pigment such vessels are in my experience always veins, i.e. the pigment travels in the direction of the blood current." See Bibl. No. 263, p. xcix.

[5] See *Description of Pedigree Plates*. See also Bibl. Nos. 87, 158, 258, 285.

of these histories may suggest that in some cases *retinitis pigmentosa sine pigmento* is merely an early stage of typical retinitis pigmentosa, but this cannot be assumed and is certainly not true of all cases. Of interest in this connection is the case described by Hocquard[1] of a man aged 21 whose right fundus showed one oval spot of pigment only, lying along the trajectory of a vein, his left fundus showed two or three small pigment deposits of typical shape; the man died of malignant scarlet fever and a *post-mortem* examination of his eye by Poncet[2] revealed a pigmented zone 15 mm. in width in the external layers of the retina[3].

To consider now the age of onset of the disease, the rate of maturity and the age at which blindness ensues. The information on these points is vague and perhaps inevitably so in most cases, but from the examination of reports it may we think be accepted that the onset is at an early age in the great majority of cases and is a rare occurrence after the age of 20 years; also we think it may be accepted that sight is very frequently lost before the age of 40 years[4]. It would be of interest to investigate whether there is not a tendency for the age of onset and age at which blindness ensues to be roughly constant within the stock, for we do find that in certain families the disease is described as congenital in all the affected members, in other families the onset is invariably late and again a very rapid course may be a characteristic feature in certain stocks.

The sort of series which can be obtained from our material omitting certain cases where the diagnosis is uncertain are as follows:

Time of Onset		Age of Blindness* in Retinitis Pigmentosa	
Congenital, before earliest recollections, or in infancy	75	0—4 years	17
		5—9 „	10
In childhood	23	10—14 „	8
In school period	14	15—19 „	9
In youth	8	20—24 „	9
Or where age is actually stated:		25—29 „	6
0—4 years	7	30—34 „	5
5—9 „	19	35—39 „	4
10—14 „	24	40—44 „	12
15—19 „	17	45—49 „	6
20—24 „	5	50—54 „	13
25—29 „	5	55—59 „	4
30—34 „	3	60—64 „	2
35—39 „	4	65—69 „	1
40—44 „	2		
45—49 „	1		
50—54 „	0		
55—59 „	1		

* Blindness for this table includes those who were described as nearly blind, those whose vision was reduced to finger counting and those whose vision was reduced to hand movements only.

[1] Bibl. No. 89. See also Fig. 7.

[2] Bibl. No. 91.

[3] This case very possibly represents an early stage of retinitis pigmentosa.

[4] Nettleship summarises the available information on this point. See Bibl. No. 251, pp. 350—6.

Retinitis pigmentosa is only exceptionally asymmetrical in its manifestations, even when the distribution of pigment is atypical and confined to one or other quadrant of the fundus it is very generally described as being the same in both eyes of the patient, nevertheless undoubted cases of unilateral retinitis pigmentosa do exist in which cases the one eye may be in all respects typical of the disease and the other eye perfectly normal. It is of course possible that more cases of unilateral defect from this source may exist than is recognised, for amongst the working class population the slow progressive loss of vision, in one eye only, may easily escape notice unless some difficulty with the sound eye brings the patient to an ophthalmological clinic, for the majority of people only consult the medical profession when they are in pain or their daily routine is being hampered in some way. Nevertheless we feel assured that there is no appreciable amount of undetected unilateral retinitis pigmentosa. The following cases are all we have been able to find in the literature illustrating the condition. Nettleship[1] in 1908 reviewed previously published cases and reports a case of his own in a woman aged 30 who had "perfectly typical and very abundant retinitis pigmentosa affecting the right eye only"; he also describes in some detail the case reported by Pedraglia[2] in 1865, by de Wecker[3] in 1870, by Baumeister[4] in 1873, by Derigs[5] in 1882, by Ancke[6] in 1885, by Reinecke[7] in 1894, by Rosenbaum[8] in 1900 and by Gonin[9] in 1902. Of this series Baumeister's case is of special interest as the patient, a man aged 44, was not only blind in his left eye from typical retinitis pigmentosa but had been deaf since childhood in his left ear; his right eye was normal and not night-blind, his right ear was not deaf. Nettleship considered that there was no reason to suspect syphilis either from the history or from the ophthalmoscopic appearances in the cases quoted by him. Pagenstecher[10] in 1861 describes an atypical case associated with deafness in a girl aged 20; he regards her condition as primarily a choroidal affection; the right eye only was affected; three of her maternal aunts were deaf and night-blind. The case published by H. Schmidt[11] in 1874 is of interest in this connection; a peasant aged 55 had atrophy of the disc and some narrowing of the retinal vessels on the right side only, he had seen badly with this eye since childhood and it was now blind except for a small portion of the outer quadrant of the field of vision where he could still see to count fingers; his left eye was normal; two of his children had typical retinitis pigmentosa which in each case was more advanced in the right eye than in the left. Günsburg[12] in 1890 described a case of typical retinitis pigmentosa in one eye only; the patient in this case had a history of an apoplectic fit at a relatively early age.

Wilbrand and Saenger[13] in 1909 report a case of unilateral retinitis pigmentosa in a man who at the age of 46 years had V. $= \frac{6}{9}$ for the left eye which was ophthalmoscopically normal whilst his right eye could count fingers only, and had posterior cortical cataract with retinitis pigmentosa; the patient's sister was reported to be nearly blind and deaf. Jennings[14] in 1911 describes a woman aged 35 years whose right field of

[1] Bibl. No. 251, pp. 164—6. [2] Bibl. No. 51. [3] Bibl. No. 160. [4] Bibl. No. 79.
[5] Bibl. No. 112, p. 19; Plate XX, Fig. 236. [6] Bibl. No. 132. [7] Bibl. No. 179, p. 11. [8] Bibl. No. 213, p. 17.
[9] Bibl. No. 218, Case 19. [10] Bibl. No. 44; Plate XXI, Fig. 252. [11] Bibl. No. 88; Plate XVIII, Fig. 200.
[12] Bibl. No. 161. [13] Bibl. No. 264; Plate VII, Fig. 111. [14] Bibl. No. 273.

vision was contracted to within 8° of the fixation point, the disc was pale, the vessels narrowed, at the extreme periphery two or three typical deposits of pigment could be seen; her left fundus was perfectly normal; for this patient the family history was good, the parents were unrelated and three brothers had normal vision.

Mohr[1] in 1921 describes unilateral retinitis pigmentosa in a patient aged 38 who had only noticed five years previously that he saw badly with his left eye; he had posterior cortical cataract, was night-blind, and the fundus was typical of the disease in all respects in his left eye only; the right eye was absolutely normal. There was no history of syphilis and the Wassermann test was negative; the parents were unrelated and no other case of the disease was known in the family. This patient also was deaf.

It may be of some interest to mention here also the case of unilateral idiopathic night-blindness described by Magnus[2] in 1886.

Many cases might be cited in which though both eyes are affected the conditions of vision and the ophthalmoscopic appearances differ markedly in the two eyes; for example Mooren[3] in 1867 describes a case in which visible pigmentation was present in the left retina only, but the right eye of this patient had a contracted field of vision and showed other signs of degeneracy. There are not however more of these cases than are consistent with our statement that retinitis pigmentosa is only exceptionally asymmetrical in its manifestations.

To conclude this brief statement concerning the signs and symptoms of retinitis pigmentosa we must call attention to the fact that perhaps of all the signs enumerated that of narrowing of the retinal vessels, which we have not discussed in any detail, is the most universally present, and we doubt whether any case has been diagnosed in which this sign is not present to a more or less degree; moreover, it may generally be taken that the severity of the disease is in direct proportion to the lumen of the retinal vessels which gradually decrease in size, or disappear altogether in the case of the smaller vessels, as the disease progresses.

(γ) *The pathology of retinitis pigmentosa.* The subject of signs and symptoms leads us to consider the source of these manifestations of disease, how can their development be explained? In short, what do we know of the pathology of retinitis pigmentosa?

There are in this connection three alternatives to be dealt with: i. Is the disease inflammatory or degenerative in nature? ii. Is the seat of the disease originally in vascular or in nervous structures? iii. Is the disease primarily of the retina, or are the retinal manifestations only secondary to a defect of the choroidal tunic of the eye? The two latter alternatives are to some extent interdependent. Two types of evidence are available for this discussion, the evidence obtained from *post-mortem* examinations of eyes affected by the disease, and experimental evidence. We propose to consider first the evidence we have from *post-mortem* examinations of eyes affected by retinitis pigmentosa.

It is perhaps surprising to find how many anatomical examinations of this disease

[1] Bibl. No. 326. [2] Bibl. No. 143. [3] Bibl. No. 59.

have been made, for it is a condition which in itself leads to no need for excision of the eye during life, and considering the rapidity with which retinal tissues degenerate after death there are difficulties to be overcome in such an event. These very facts make it evident that some other condition is probably present, in addition to retinitis pigmentosa, in all cases upon which anatomical examinations have been made and presumably may in some respects have influenced the microscopic picture. However this may be there is a uniformity in the descriptions of certain characteristic features which is reassuring.

Amongst the many discussions of the pathology of retinitis pigmentosa based in most cases upon anatomical investigations, we would mention those of the following authors: Maes[1], Donders[2], Junge[3], Schweigger[4], Bolling Pope[5], Leber[6], Windsor[7], Landolt[8], Poncet[9], Hosch[10], Lister[11], Gonin[12], Ginsberg[13], Stock[14], Parsons[15], Knape[16], Doyne[17], Suganuma[18], Greeves[19], McKee[20], and Treacher Collins[21]. Of the cases examined by some of these investigators—Leber's patient died of typhus; one of Landolt's cases died from cirrhosis of the liver and kidneys; Poncet's case died of malignant scarlet fever and is of some special interest as being the same case as that described by Hocquard (see Plate II, Fig. 7) which showed during life a very slight development of pigment in the retina; Lister's case is of interest from the fact that the patient had been totally blind for some years before his death at the age of 60 years, and thus the disease is seen in a very advanced stage; the case described by Gonin was unilateral; Ginsberg's patient died from tuberculosis; Stock's case was associated with syphilis; Knape's case had a detached retina and there was a development of pigment on the detached portion of the retina; Suganuma examined an eye which had had to be removed on account of a hypopyon ulcer and so on.

The chief features of the microscopic picture, described very constantly as being present to a more or less degree dependent upon the age of the patient and stage of the disease, in these and other cases are:

i. Disease of the retinal vessels; the walls are thickened, sclerosed and deeply pigmented, the lumen partly or altogether obliterated; the smaller vessels may be reduced to fibrous cords embedded in hypertrophied connective tissue.

ii. Atrophy of the nervous elements of the retina. This condition is the most advanced in the external layers of the retina and increases in intensity from the centre towards the periphery. In a severe case, such as Lister's, the layer of rods and cones was everywhere absent and was replaced by laminated fibrous tissue in which numerous oval nuclei could be seen; outside the central area of this case all traces of the normal structure of the retina were lost.

iii. Hyperplasia of the connective tissue framework of the retina.

[1] Bibl. No. 43. [2] Bibl. No. 36. [3] Bibl. No. 39. [4] Bibl. No. 41. [5] Bibl. No. 46.
[6] Bibl. No. 68. [7] Bibl. No. 70. [8] Bibl. No. 77. [9] Bibl. No. 91.
[10] Bibl. No. 90. [11] Bibl. No. 225. [12] Bibl. No. 222. [13] Bibl. Nos. 221, 247.
[14] Bibl. No. 255. [15] Bibl. No. 252. [16] Bibl. No. 250. [17] Bibl. No. 268.
[18] Bibl. No. 286. [19] Bibl. No. 280. [20] Bibl. No. 293. [21] Bibl. No. 318.

iv. Pigmentation of all the layers of the retina which is especially marked along the course of the blood vessels; the pigment arises from the migration and proliferation of the cells of the pigment epithelium and all that remains of the pigment epithelium as such, in advanced cases is a short row of pigment cells here and there. Wherever pigmentation is found there the rods and cones are absent and the retina is atrophied, but the converse does not hold and it is by no means the case that where the retina is atrophied there migratory deposits of pigment will be found. Hence it may be assumed that pigmentation may follow upon degeneration but does not precede it.

v. Adhesions between the atrophied retina and the choroid.

vi. Choroidal changes. The changes which may be seen in the choroid are degeneration, amounting in some severe cases to total disappearance of the chorio-capillaris, and sclerosis of the large choroidal vessels; but the observations in these respects are by no means constant, they differ markedly from case to case and in some specimens the choroid is reported to be absolutely normal.

The deductions from these observations have varied from time to time; the earlier authors, for example Donders, Landolt, Bolling Pope, Windsor, De Wecker[1] and others believed the lesion to be primarily of a chronic inflammatory nature, they considered that the seat of the lesion was in or around the walls of the retinal vessels and explained the atrophic condition of the retina as the result of a gradually failing blood supply. This view came to be almost entirely discarded as it was recognised that certain distinctive features of inflammation were absent and indeed many observers have definitely stated that they find no trace of inflammation. (See Gonin, McKee, Suganuma, Aubineau[2], etc.) For many years it has been almost unanimously agreed that the disease should be regarded as of an atrophic or degenerative nature, but opinion is by no means agreed as to whether the degenerative process originates in the chorio-capillaris, the layer of the choroid which is entirely responsible for the nutrition of the outer layers of the retina, whether it originates in the nervous elements of the retina itself, manifesting first in the layer of rods and cones, or whether some defect of the retinal vessels precedes the degeneration of the nervous elements of the retina.

For a period the theory that the chorio-capillaris was the most probable source of the retinal disease was held by the majority of inquirers and was consistent with the fact that the external layers of the retina show severe changes at an early stage of the disease; Nettleship held this view, also Gonin and others; and on the whole *post mortem* appearances had justified this conclusion, even though certain observers, of whom we may mention Schweigger, had found that deposits of pigment in the retina could and did occur quite independently of any changes in the choroid. More recently, as material has accumulated, the growth of opinion has been in favour of the defect being regarded as a primary atrophy of retinal elements, and we would advise all interested in the subject to read the very suggestive paper by Treacher Collins from this point of view; he points out that a number of microscopic examinations have been made in which the choroid was entirely normal, and he considers that only by a

[1] Bibl. No. 58. [2] Bibl. No. 219.

destruction of the rods and cones, thereby leaving gaps in the external limiting membrane through which pigment grains, attracted by the action of light, can migrate and so reach the internal layers of the retina, can the mechanism of pigmentation of the retina be explained. No theory yet advanced seems to entirely satisfy all conditions, and repeatedly the situation has arisen of another "beautiful theory killed by a nasty little fact."

Doyne's remarks on the pathology of retinitis pigmentosa are also very interesting; he felt convinced that the condition was not a simple atrophy, and gives many reasons for this statement; he suggests some exudative infiltration of the retina as the source of the defect, and considers the possibility of some abnormal condition in connection with the mechanism by which visual purple is secreted.

To consider now what experimental evidence is available bearing on the subject.

Four investigations along these lines may be mentioned—Wagenmann[1], Berlin[2], Krückmann[3] and Capaunner[4]—who cut posterior ciliary arteries in the rabbit, guinea-pig or frog, leaving the retinal vessels intact. This operation was followed by atrophy of the corresponding part of the choroid and by degeneration and pigmentation of the outer layers of the retina over that part of the choroid which had been supplied by the cut vessels; Capaunner observed changes in the case of the rabbit three days after the operation had been performed. On cutting only the retinal vessels, leaving the posterior ciliary vessels intact, no degeneration or pigmentation of the outer retinal layers took place.

These experiments demonstrate the dependence of the outer retinal layers upon the choroidal circulation for their nutrition, they further demonstrate that pigmentation of the retina can be produced by interference with the choroidal circulation in certain animals, but they do not prove that retinitis pigmentosa in man is produced primarily by a defect in the choroidal blood supply.

Pigmentation of the retina with disturbances of the corresponding region of the chorio-capillaris has also been observed to develop as a result of optico-ciliary neurectomy in man[5].

The little that we know of the determining factor in the production of the early and marked symptom of night-blindness does not contribute much to our knowledge of the pathology of retinitis pigmentosa, yet it is not without interest in this connection. Schultze[6] first suggested that the rods of the retina were concerned with the sense of light and space, and the cones with colour vision; Parinaud[7] then developed the theory that night-blindness was due to a change in the visual purple and in the rods. The tradition that hepatic organo-therapy was of specific value in certain cases of night-blindness, combined with the observed reaction between bile pigment and visual purple in the test-tube, appeared to support this theory. Hess[8], however, in an extremely interesting paper, strongly opposes this view and pronounces that night-blindness is not due to a lesion which is confined to the rods; further, Hess broke down the popular

[1] Bibl. No. 164. [2] Bibl. No. 71. [3] Bibl. No. 204. [4] Bibl. No. 173.
[5] See Studer, Bibl. No. 236, and Treacher Collins, Bibl. No. 318.
[6] Bibl. Nos. 57, 73. [7] Bibl. No. 130. [8] Bibl. No. 269.

tradition that hens were night-blind and was unable to bring about night-blindness in hens by means of artificial icterus produced by ligature of the bile duct; he found also that such artificial icterus in the rabbit left the visual purple unchanged.

Though the source of night-blindness may be regarded still as somewhat obscure, it is of significance that on examination of the retina in animals it is found that rods are more numerous in cave dwelling animals than in those living in the open and that in night birds rods preponderate. The retina of the lizard and snake are said to have cones only.

Thus the knowledge which we have of the pathology of retinitis pigmentosa tends to emphasise the complex nature of the condition, and perhaps suggests that the group of cases diagnosed as such may not be really homogeneous, even though there is great unanimity in the clinical picture of the cases described and in the slow progressive nature of the disease terminating inevitably in blindness provided the patient lives long enough. Experience is invariable also in reporting the result of treatment to be in all cases unavailing, if we except the improvement after trephining reported by Mayou[1] and by Kirkpatrick[2] and some temporary improvement noted occasionally after use of the constant current.

(δ) *Diseases and defects found in association with retinitis pigmentosa.* The significance of the presence (or absence) of associated defects in all cases of inheritable disease is only gradually becoming recognised, and from this point of view the Usher series of pedigrees is of great value, for the author has systematically enquired for information on this point from his patients and their relatives. It is only permissible to make very rough estimations of the frequency and character of associated defects from our material as a whole, because the majority of authors make no statement on the subject, and we feel sure in many cases have not investigated the facts. We have heard repeatedly from Karl Pearson and other writers of the pedigrees of general degeneracy in which an inherent mental instability expresses itself in a variety of ways in the different members of the stock—thus one member may be insane, another irritable and passionate, another a somnambulist, an alcoholic, a suicide and so on—the manifestations of the defect are varied, but we may take it that the tissue or cells in which they originate are the same, and we have no reason whatever to expect that in such a pedigree certain other inheritable defects, say haemophilia, will occur. May we expect to find cases of retinitis pigmentosa noted in such a pedigree?

Again to turn to pedigrees of more definite structural developmental defects such as hare-lip and cleft palate; we are at once struck by the number and character of the associated defects[3] which here again are markedly restricted to structural defects in the development of limbs or organs or parts of the body, produced in many cases we know by amniotic adhesions and in other cases perhaps by some other, not necessarily

[1] Bibl. Nos. 305, 309.

[2] Colonel Kirkpatrick trephined one eye for a man suffering from retinitis pigmentosa who was so much benefited that he returned two years later asking for the operation to be performed on the second eye.

[3] For an analysed table of deformities reported in association with hare-lip and cleft palate see *Treasury of Human Inheritance*, Vol. I., pp. 93—107.

mechanical, arrest or interference with the normal development of normal tissues into their characteristic forms. We should expect in such pedigrees to find such eye defects occurring as microphthalmos, anophthalmos, coloboma iridis and others; we should not expect to find more than a chance case of haemophilia. Should we expect to find retinitis pigmentosa?

In the case of haemophilia there appear to be no characteristically associated inheritable defects, and we are sure that if such existed they would not fail to be indicated in the memorable section in the first volume of this publication by Bulloch and Fildes. We may however refer here to the very interesting suggestion thrown out by Voorhoeve[1] as a possible explanation of a pedigree in which the frequently related blue sclerotics, brittle bones and easily dislocated joints are seen associated with haemophilia and other defects; he considers the possibility of an inherent defect in the mesoblastic tissue showing itself in a variety of structures developed from it. The theory is ingenious and worth bearing in mind, though so far as the association with haemophilia is concerned it seems unlikely that a true haemophilic who repeatedly broke his bones and dislocated his joints would live to talk about it.

The extremely illuminating experimental work of Stockard[2] on the production of structural defects by varying the developmental rate at certain critical periods is of interest in this connection. He is able to produce a great variety of associated defects, the character of which are in direct relation to the particular moment in the development of the organism at which his interference (which concerns itself with temperature and oxygen supply) is applied. He comments on the frequency and variety of defects in the eyes thus obtained. The paper is teeming with interesting suggestions, but it is only possible here to quote from it a few passages to indicate the possible application of the author's observations to our problems. Thus on pp. 233—4 "When the optic vesicle does not grow out from the brain at a definite developmental moment it is subsequently unable to grow out and develop normally or it may be unable to grow out at all. I have definitely inhibited development during this period in a large number of experiments and have either suppressed or modified the development of the eye. It may be concluded that such an organ as the eye is not only derived from a definitely located primordia, but must also be derived during a limited moment of development." And again on p. 243 "The periods of arrest necessary to induce the eye and the brain modifications are so close together or so nearly the same, that one generally finds combinations and mixtures of the defects among the same experimental groups of embryos. Arrests at the earlier moment give a majority of eye conditions, many without brain involvements, while arrests at the slightly later stage give a majority of brain modifications, a few with fairly well-formed eyes. The individual variations in developmental moments among the embryos of a group also tend to contaminate the results and give mixtures of the two classes of deformities."

From the nature of the case the defects obtained experimentally must be of a rather gross character, but it is evident that finer shades of interference at critical moments for certain organs might well produce such defects as we are familiar with

[1] Bibl. No. 315. [2] Bibl. No. 328.

in human development. Is it then conceivably possible that the origin of the defect in the case of some of our inheritable diseases is in an inherent tendency to delay or antedate the critical moment of development for certain structures?

Thus it is of considerable interest to examine what other defects are found in association with retinitis pigmentosa and to enquire whether they throw any light on the condition with which we are dealing.

The first point which strikes one on looking through the material is the number of pedigrees in which no associated defects have been noted, and we draw especial attention in this connection to the extensive pedigree worked out by Nettleship (Plate I, Fig. 1B) in which no fewer than 19 sibships contain affected members, the total number of affected individuals in the stock numbering 39; the author made a special note of the fact that all members of this stock were free from any other defect. Other examples of pedigrees in which retinitis pigmentosa is extremely prevalent and is not apparently associated with any other defect may be seen in Fig. 3 and Fig. 5. If we glance at the Usher series in which we know this factor has been considered throughout we find that on the whole the view is supported that a considerable amount of retinitis pigmentosa occurs in sibships which are free from all other inheritable defect. On our whole series, omitting certain very atypical or doubtful pedigrees, we find 656 individuals (out of a total of 919), taken from 329 sibships, affected with retinitis pigmentosa without a single case of associated disease *noted* in them, or in their normal siblings so far as information concerning them is given but too frequently all statement of the siblings is omitted or is very incomplete, and we feel assured that in a large number of cases associated defects in the affected individual have not been inquired for and that with more complete information the numbers given above would be perhaps markedly reduced.

When we consider what associated defects have been observed the only two conditions which are found to occur with any marked frequency in association with retinitis pigmentosa are deafness, often deaf-mutism, and idiocy or some type of mental defect or defect of the central nervous system, and of these the question of associated deafness is of rather special interest from the fact that the observed high degree of association is concerned rather with retinitis pigmentosa in the individual pedigrees in which it occurs than with retinitis pigmentosa as a whole.

There are in our material 96 cases of retinitis pigmentosa associated with deaf-mutism or deafness out of a total of 919 cases; that is to say, on the whole series 10·4 % of our cases have these two defects.

If now we consider only those pedigrees in which deafness occurs as a complication in at least one case of retinitis pigmentosa we find that for this series of pedigrees no less than 74·3 % of our cases are either deaf-mutes, or are deaf. And if we further examine the Usher pedigrees in which we know that the presence of deafness was definitely inquired for we find that if we take only the pedigrees in which one case of deafness occurs as an associated defect, 100 % of the cases of retinitis pigmentosa from such pedigrees are so associated. Further, we notice that the degree of deafness, or at any rate its time of onset, appears to be more or less constant within the stocks in

which it occurs, for where mutism is also present, which we take it means that deafness was complete before the age of 7 years, then mutism is present in all cases within the stock in which deafness occurs. The case of Baumeister already referred to, in which the combined defects were present in the left eye and ear only, is of special significance in this connection as indicating the intimate nature of the association. When we consider whether deafness may occur in the members of an affected sibship who are free from retinitis pigmentosa we find seven such cases reported, see Figs. 83, 95, 110, 201, 213, 239 and 246, but in some of these the information was very scanty and the eyes of the otherwise normal deaf members had apparently not been examined. We think we may fairly conclude that where deafness occurs in relation with retinitis pigmentosa in any member of a stock this defect will almost invariably be associated with any case of retinitis pigmentosa that occurs in the same sibship and will tend to be associated also with cases which occur in other sibships of the stock.

An anatomical examination of the ear from a case of deafness associated with retinitis pigmentosa would be of great interest and would possibly throw much light on the question of the etiology of the disease; so far as we have been able to discover no such examination has yet been made.

The double defect of deaf-mutism and retinitis pigmentosa must undoubtedly tend to be a bar to marriage but it is a little surprising to find that omitting the extremely doubtful case of Oakley's (see Fig. 86) we have only one case of associated deaf-mutism for which the parents were not both normal; this occurs in a case described by Chaillous (see Fig. 177) in which a man with retinitis pigmentosa married a normal unrelated woman and had one child, a deaf-mute son with retinitis pigmentosa. There are a few cases on record in which persons with this combination of defects have married and were reported to have normal children, and one case, described by Nettleship (see Fig. 87) in which a woman so afflicted married an unrelated normal man and had two children, a normal son and a daughter with retinitis pigmentosa. There is a markedly higher percentage of consanguineous marriages amongst the parents of these doubly afflicted persons than exists for the parents of our general population of affected sibships; we shall return to this point again later when discussing the influence of consanguinity on the production of retinitis pigmentosa.

If we take now the group of associated defects comprising idiocy, epilepsy, and any form of mental defect or defect of the central nervous system we find a rather similar state of affairs to a much less marked degree; our information concerning such a group is probably even more incomplete than in the case of deafness but such positive information as we have gives us 37 cases in which one or more defect of this group is associated with retinitis pigmentosa. If then we consider the affected members of our whole series this gives us a percentage of 4·0 cases in which this combination of defects occur; if on the other hand we consider those pedigrees only in which at least one affected individual has a further associated defect from this group we find for the affected members of these pedigrees a percentage of 34·6 cases in which this combination of defects occur. The impression given by a cursory examination of the occurrence of defects of this group in the pedigrees, is that they tend to occur more in the normal

members of the affected sibships and to be to a far less degree confined to the affected members or even to the affected sibships than is the case with deafness.

It is not possible on the evidence available to give any opinion as to whether the occurrence of defects of this group in the normal members of the pedigrees indicate or do not indicate a degeneracy latent in the stocks of which the retinitis pigmentosa is only another manifestation.

A rarely associated defect which has received an amount of reference out of all proportion to the frequency with which it occurs is polydactylism, but the relationship is of interest as indicating that the link when it does occur is of great intimacy as in the case of deafness. Thus we have in our pedigrees nine cases of polydactylism associated with retinitis pigmentosa as well as two cases of polydactylism, in the siblings of one patient, who died before the condition of the eyes was known, in five small pedigrees[1]; two cases of retinitis pigmentosa in these stocks were not polydactylous. Further similar histories of this combination of defects in isolated cases are given by Herrlinger[2], Stör[3], and others.

The only other disease or defect which occurs in association with retinitis pigmentosa with sufficient frequency to be of any interest here is glaucoma, the combination is relatively rare but such cases as we have been able to collect in which it occurs may be seen in the description of Figs. 244, 245, 246, 247, 248, 249, 250 and 251, where eleven cases of glaucoma are described in patients suffering from retinitis pigmentosa and two cases of glaucoma in the siblings of such patients.

We think we may fairly conclude that retinitis pigmentosa occurs largely as a single affliction unaccompanied by other disability; the fact that this is the position in some of our fully worked out pedigrees in which the disease occurs with marked prevalence through several generations perhaps explains the existence of such pedigrees, and it may well be that stocks in which cases occur in association with further defects tend rapidly to die out.

We may further conclude that wherever deafness is found in association with retinitis pigmentosa the link is a very close one and the two disabilities may with a high degree of probability be expected to occur inseparably within the stock.

It is of interest, in consideration of the theory that atrophy of the chorio-capillaris, the exclusive source of the blood supply to the external layers of the retina, is primarily responsible for the disease, to search for other defects of the vascular system within such stocks but we can find no widespread or significant evidence of such an association. Nettleship has collected all available cases in which the onset of the disease had been attributed to severe haemorrhage and Usher made frequent enquiries for such a history, but such cases are very rare and may have quite other explanations; there is no evidence of early or severe arterio-sclerosis in these stocks, if we omit Bordley's[4] entirely anomalous case (see Fig. 6); there are isolated and rare cases described of senile gangrene, or Raynaud's disease, or cold hands and feet or chilblains all of which are perhaps defects of the vaso-motor system due to hyperactivity of the sympathetic

[1] See Figs. 24, 96, 114, 205, 237. [2] Bibl. No. 203, Case 14. [3] Bibl. No. 52. [4] Bibl. No. 245.

constrictor nerves rather than primarily vascular defects. And further there is no evidence of any associated heart disease apart from the again anomalous case of Dor[1] (see Fig. 256).

Certain cases have occurred which have led to the suggestion that acute illness or infections or nervous shocks may determine the onset of the disease which would have otherwise remained latent, or may conspicuously produce an exacerbation of symptoms and modify its course. The story described by Nettleship[2] (see Fig. 215) in which the disease followed scarlet fever in five siblings is the most significant of these cases; other interesting histories by the same author writing on *Some of the exciting causes of retinitis pigmentosa* bear on this point. For further cases amongst our series which have been attributed to maternal shock, or fright, or to some acute illness or severe haemorrhage, or at any rate were associated with one or other of these conditions, see *Description of Pedigree Plates*, Figs. 10, 17, 79, 99, 140, 148, 151, 163, 168, 172, 184, 215, 217, 235, 247. No doubt many of these cases are merely coincidences for the average patient with his relatives likes to be able to attribute any disabilities which occur to a definite cause; an example of this may be seen in Fig. 173 where there was a difference of opinion as to whether retinitis pigmentosa in two siblings was the result of their snowballing or was due to slaps on their heads administered by a drunken father. Nettleship was of the opinion that there were enough of these associations on record to warrant a careful investigation with regard to their possible significance on the part of subsequent investigators; he suggests the possibility that such cases might be an indication of the existence in certain stocks of an hereditary tendency to disease of small arteries, say of the choroid, which may under favourable conditions remain latent through life but which might become patent if the resistance of the individual be lowered by toxic illness or by loss of blood.

We are of the opinion that Usher's investigation does not give much support to the view that there may be any significance in these associations.

(ε) *Racial and geographical distribution of retinitis pigmentosa.* It is not possible to give any definite statement as to the relative frequency of retinitis pigmentosa in different races or countries; the lack of published accounts of the disease in any particular country may by no means be taken to indicate the rarity of the disease in the corresponding race. We may probably take it that the condition occurs more or less uniformly in the countries of Europe. In America there is some indication that perhaps the disease may be less prevalent; at a meeting of an American Ophthalmological Society, reported in the *Ophthalmic Record* for 1911, p. 267, Saxlsaid "cases of retinitis pigmentosa do not seem to be frequent in this country"; Owen agreed that it was an uncommon condition, Loeb had seen two cases in 250 patients since his hospital clinic had started. We can attach little importance to these vague statements but, added to the fact that we have relatively few American cases in our collection, they suggest that further information on the subject would be of interest. We think it may possibly be accepted that the condition is rare in the coloured races of America; omitting Bordley's[3] extremely interesting though anomalous case in the negro we can find very

[1] Bibl. No. 267. [2] Bibl. No. 251, pp. 159—61. [3] Bibl. No. 245, Fig. 6.

little evidence of the disease amongst these races, it must however be borne in mind that races differ markedly in the way they tolerate an affliction, to some, illness when it comes, particularly if it be of a slow progressive nature, tends to be borne in silence and to be accepted as the hand of fate; such cases are not taken to the hospital to be treated nor do accounts of them reach the medical press. Ayres[1] writing in America in 1892 describes retinitis pigmentosa in a negro and states that it is the only case he has ever seen in a coloured race; Jones[2] makes a similar statement on describing the condition in a mulatto girl.

Roy[3], writing on the African negro, states that they see very well at night and that he has noticed this characteristic also in the Indo-Chinese, Malays, Redskins and even in Hindoos; we should like to see the result of some definite test for light sense in these races. Junker writing in 1866 says that he has never seen a negro affected with night-blindness[4].

The case of China also is of interest for it has been repeatedly stated that night-blindness is more common in China than in Europe on the basis, we believe, of a report to this effect taken from Jesuitical literature and published by Bergen and Weise[5] in 1754. We hope to be able to obtain some information on the prevalence of retinitis pigmentosa in China before going to press. With regard to India, Kirkpatrick[6] writes "Retinitis pigmentosa is extraordinarily common in the east and accounts for 21 °/₀ of all diseases of the choroid and retina; a history of consanguinity can be obtained in 87 °/₀ of the cases"; he states further that the pigmentary and atrophic changes found are probably more extreme than those met with in Europe and that the whole of the fundus is involved at a comparatively early date. Kirkpatrick's report is very interesting but we must remember that the Indian patient may have to save up for years in order to have money enough to take the journey to the nearest hospital, and that the medical officer there is thus likely to see only the severe cases. Well authenticated retinitis pigmentosa has we believe only twice been recorded in animals; as early as 1864 van Biervliet and von Rooy[7] observed it in horses and more recently Magnusson[8] has reported an exceedingly interesting pedigree of the condition in dogs[9]; the consanguinity in the matings for this experiment was much closer than anything that can ever occur in man, thus of the three affected sibships one was the offspring of half siblings, one the offspring of siblings and the third was the offspring of an affected mother mated with her grandfather who was the father of both her parents. Night-blindness was first noticed in these dogs at about the age of 6 months and one dog became completely blind in four years; a *post-mortem* examination in one case showed a condition very similar to that described for man.

(ζ) *Statistical Observations. Consanguinity.* It has been the custom for this publication to collect material for the student of heredity and to give some general description of the condition which is to be investigated. The subsequent analysis of

[1] Bibl. No. 169. [2] Bibl. No. 314. [3] Bibl. No. 320.

[4] Bruns saw three cases of retinitis pigmentosa in 1113 negro patients at an eye clinic in two years. Bibl. No. 185. [5] Bibl. No. 20. [6] In Elliot's book, Bibl. No. 322, p. 390.

[7] Bibl. No. 48. [8] Bibl. No. 276. [9] Fig. 185.

the material must be a heavy task and before any attempt at a numerical estimation of the intensity of inheritance be attempted a critical survey of each pedigree will need to be made. Pedigrees in which single cases alone occur should be omitted; we do not wish to underestimate the value of such pedigrees which may throw much light on the nature of the affection when all the associated defects and the characteristics of the stock are noted as fully as in Usher's cases, but in them the defect is not an inherited one and may well be secondary to a toxaemia or to some defect of other organs in the individuals, indeed from what we know of the range of variability in all organs in the general population we should expect that in certain exceptional cases an extreme variation from the normal in some respect may occur in the development of any tissue which may well be incompatible with the needs of the functioning organ developed from it. Such isolated cases occur in every inheritable disease as we know from albinism, cataract, phthisis and diabetes to give only a few examples, they in no wise weaken the importance and clinical significance of the hereditary nature of such diseases in certain stocks, nor to give another example can any of us regard the isolated occurrence of genius as any bar to our acceptance of the view that ability is markedly inherited.

Again, before the analysis of the material as a whole can be considered the age of onset in each pedigree will need to be examined, and in cases for which the 'normal' members were below the age at which the disease tends to occur the whole sibship should be rejected until it is known from an examination of the entire population in what proportion these undetermined cases should be divided amongst the affected and unaffected; sibships in which members died young or in infancy should be similarly treated. May we assume that pedigrees in which the disease is always congenital are truly homogeneous with those in which the disease always developed at say about the age of 17 years?

We must further point out that there appears to be some very fundamental difference between such pedigrees as for example Figs. 1B, 3 and 5 in which the defect is very prevalent and is invariably transmitted by affected individuals the normal members of these stocks bearing normal offspring only in every case, and pedigrees such as Figs. 50, 57, 156, 212 and 225 in which the disease may miss one generation or more and is transmitted through normal members of affected sibships. We cannot in the present state of our knowledge feel assured that a material containing pedigrees of a defect showing this variety in its mode of transmission is homogeneous. If we attempt to keep these two groups separate in which group are we to place the many single sibships given to us in which one parent was known to be affected?

Thus when we come to consider the possibility of an exact analysis we realise painfully our weak points and the depths of ignorance yet to be overcome before we can expect the statistician to use his tools and give us facts that we can insist upon; nevertheless we are satisfied that the collection as it stands is of value as illustrating the varied manifestations and complex nature of retinitis pigmentosa and the danger of pronouncing upon the condition in the individual met with in the out-patient department from a knowledge of a few pedigrees only and without fully investigating the family history of the individual.

With this caution and repeating that we cannot, in the present state of our knowledge, insist upon the significance of the figures given, we offer some suggestions based on the material as a whole, with a few doubtful or anomalous cases omitted, relating to (i) the influence of consanguinity in the parents on the production of retinitis pigmentosa in the offspring; (ii) the proportion in which the sexes are affected and transmit the disease; (iii) the proportions in which the offspring of affected and of non-affected parents tend to be affected; (iv) the average size of families of affected and unaffected parentage.

Considering first the affected individual apart from the sibship and examining into the sex and parentage we find a very significant preponderance of males; where the sex is given we have 454 males and 363 females affected, and 373 males and 362 females unaffected. Thus $55{\cdot}6 \pm 1{\cdot}2\,\%$ of the affected population are males, or we have an excess of 11 males in every hundred of such a population; this sexual incidence tends to support statements made repeatedly by other workers. In a large percentage of cases both parents of an affected individual are normal and it is not possible from the pedigree to say through which of them the disease has been transmitted but in 400 cases we have information on this point and it appears that:

75 affected mothers have handed on the disease to 183 children. 56 affected fathers have handed on the disease to 96 children. 36 normal mothers have transmitted the disease to 76 children. 25 normal fathers have transmitted the disease to 45 children. 30 affected mothers and 44 affected fathers have only normal offspring. These figures we think may be taken to suggest that though the male tends to become affected more readily than the female, he is less liable to transmit the disease to his offspring, for on the average the father only transmits the disease to 1·7 of his children whilst the mother transmits it to 2·3 of her children, and further a considerably higher percentage of affected fathers do not transmit the disease at all. This point will be referred to again later.

Consanguinity in the parentage has been urged again and again as one of the most important etiological factors in the production of retinitis pigmentosa and indeed when we come to examine our affected population with regard to this point we find that $27{\cdot}2\,\%$ of the individuals are the offspring of consanguineous marriages, or that $25{\cdot}8\,\%$ of the affected sibships are the result of consanguineous parentage; these figures agree closely with the values given for albinism by Professor Pearson who found that $29\,\%$ of albinos of all classes were the result of consanguineous marriage. If we limit our affected population to cases of retinitis pigmentosa from sibships in which at least one case of deafness occurs we find that $40{\cdot}2\,\%$ of such selected individuals have a consanguineous parentage, or if we limit our population to cases from sibships in which at least one case of mental defect, idiocy or defect of the central nervous system occurs we find that $37{\cdot}7\,\%$ of such affected individuals have a consanguineous parentage. Thus with an increase in the percentage of consanguinity there appears to be an increase in the defect resulting.

On considering the amount of consanguinity in marriage in the general population Miss Elderton[1] concluded from her analysis of all available material that "it seems

[1] '*On the marriage of first cousins*,' pp. 20—24. *Eugenics Laboratory Lecture Series*. London 1911.

unlikely that the percentage of first cousin marriages can be greater than 3 among all classes in England." The factor, as demonstrated on material collected in the Galton laboratory and elsewhere, varies from class to class being greater for the professional and upper classes than for the working class population. Clearly then the numbers given above are of great significance; we will now examine what proportion of the offspring are affected when there is and when there is not a history of consanguineous marriage.

Omitting all isolated cases and taking only those sibships for which complete information of the number of affected and normal individuals is given, dividing also the numbers who died young or were at the time of observation below the age at which the disease usually appeared in that family in the proportion of the affected and normal individuals found for completed sibships in which such cases do not occur, we get the following table:

Percentage of Offspring Affected

	No. of Sibships	Average size of Family	Percentage
No Consanguinity			
Mother Normal, Father Normal ...	98	6·3	45·6 ± 1·4
Mother Normal, Father Affected ...	45	4·5	25·6 ± 2·1
Mother Affected, Father Normal ...	67	4·8	47·5 ± 1·9
Consanguinity			
Mother Normal, Father Normal ...	54	6·8	44·7 ± 1·8
Mother Normal, Father Affected ...	13	3·2	38·1 ± 5·1
Mother Affected, Father Normal ...	9	4·2	[31·6 ± 5·1]

Now the numbers given for cases in which both parents were normal are not comparable with those for which one parent was affected, for the latter cases include sibships in which there were no affected offspring and when both parents were normal it was not possible to detect those cases in which one or both of them had the disease latent but produced only normal offspring, but the table appears to support our suggestion that the female more readily transmits the disease to her offspring than does the male and further although consanguinity in parentage undoubtedly produces an increase in the number of affected sibships in the population, only in the one series of cases for which the mother is normal and the father is affected do we possibly find evidence of an increased proportion of affected members within the sibship as we pass from the non-consanguineous to the consanguineous groups; we may perhaps explain this case on the assumption that the affected father does not readily transmit the disease but his wife, if chosen from the same stock, tends to increase the proportion of his affected offspring. We regret that the number of sibships for the consanguineous group is here so small that we are not able to insist upon the percentage given for it.

If we now for comparative purposes consider only sibships in which affected members

occur and take the two groups in which neither parent or one parent is affected we find:

Percentage of Offspring Affected

	No Consanguinity		Consanguinity	
	No. of Sibships	Percentage	No. of Sibships	Percentage
Both parents normal ...	98	45·6 ± 1·4	54	44·7 ± 1·8
One parent affected ...	74	53·6 ± 1·7	16	50·0 ± 4·5

This condition of things has not been found for other diseases which have been investigated. Thus Fay[1] in discussing deaf-mutism in America states that when one or both parents are affected and consanguineous 30 °/₀ of their offspring are affected, but when there is no consanguinity only 8 °/₀ of their children are deaf-mutes. Professor Pearson has found for albinism that when one parent is albinotic and there is consanguinity 32 °/₀ of the offspring are albinotic whilst only 14 °/₀ are affected when there is no consanguinity; when neither parent is albinotic but consanguinity is present 40 °/₀ of the offspring are affected, when there is no consanguinity the number is reduced to 34 °/₀.

(η) *Diseases allied to Retinitis Pigmentosa.*

Chorio-retinitis. We have included in our series only two pedigrees[2] described by the authors under this title, which are of some interest and appear to be undoubtedly allied to retinitis pigmentosa, but in which choroidal changes are a marked feature of the ophthalmoscopic picture. We have found some difficulty in deciding what should and what should not be included here for the group is ill-defined and a graduated series of cases might be arranged in which changes are present in both tunics, at one end of the scale choroidal changes predominating but becoming less marked and the retinal changes relatively more marked as we go down the scale until we find the typical picture of retinitis pigmentosa.

Retinitis punctata albescens. This condition, named by Mooren[3] in 1882, is of great rarity and the number of cases on record are too few to be of any interest from the point of view of its heredity, but it is unmistakably allied to retinitis pigmentosa and when an anatomical examination of the condition has been made may help to throw some light on the etiology of that disease. The defect is found in several members of a sibship, which is the more significant in the light of its extreme rarity, and affects both sexes; it has never been observed in more than one generation in any family but is noted relatively frequently in pedigrees in which retinitis pigmentosa has occurred. The chief characteristic of retinitis punctata albescens is the presence of white dots in the fundus, but there are other conditions in which light spots are seen in the fundus such as those due to colloid bodies, due to honeycomb choroiditis or even due to Gunn's

[1] Fay, E. A. *An Inquiry into the Marriages of the Deaf in America*, p. 108. Washington 1898.

[2] See Fig. 256, Dor's Case, and Fig. 257, Pollot's Case.

[3] Bibl. No. 114, p. 217.

crick dots, so that care is necessary in making the diagnosis, though Nettleship says the condition is quite characteristic and once seen is unmistakable; the dots are deep to the retinal vessels which invariably pass in front of them. To quote from Nettleship[1] "several conditions have received this title; the name should be restricted to the cases, apparently quite rare, in which the fundus is sown pretty evenly with innumerable discrete white dots entirely free from pigment, dull or dead like white paint, affecting the central region as well as or even more than the periphery, apparently dating from birth or early life and remaining so far as is at present known stationary; the dots are always small and may be invisible by the indirect method." Nettleship kept certain of his cases under observation over a long period of years, in some cases he notes no change in the fundus but in one case[2] he observed the entire disappearance of the white dots with the development of several pigmentary deposits typical of retinitis pigmentosa; in the sister to this case who was similarly affected, he observed a diminution in the number of the white dots. One other such observation has been reported by Gradle[3] who noted *retinitis punctata albescens* in a woman aged 29 associated with pigmentation of the retinal periphery; eight years later the white spots had disappeared.

Other characteristics of the condition are night-blindness which is almost invariably present from an early age; the retinal arteries may be slightly narrowed but are never markedly so; the discs may be a little pale, or may be normal; the fields are usually contracted in a dim light and may be so in a good light; and finally the visual acuity in a good light may be full or may be markedly diminished.

Sixteen small pedigrees in which *retinitis punctata albescens* occurs are given in Figs. 269—284 of our series and of these, the cases described by Spengler[4] and Diem[5] are atypical in the absence of night-blindness, the case described by Nettleship and Collins[6] is atypical in the late onset of night-blindness. Other references to the condition are given in the Bibliography[7]. The case described by Cohen[8] is of interest as it is the only case reported of *retinitis punctata albescens* in more than one sibling in a coloured race, but the condition described is not entirely consistent with Nettleship's definition given above. The disease certainly occurs in India for Kirkpatrick has noted one and possibly two cases amongst the 327 cases of disease of the choroid or retina seen at Madras during the years 1914—1918. We believe that several cases have recently been reported in a Japanese ophthalmological journal but we have been unsuccessful in our attempts to procure it.

Choroideremia. This may almost certainly be described as a developmental defect in the complete form of which the choroid is entirely absent; the defect in such cases appears to have taken place at a very early date before the first signs of the development of the chorio-capillaris at the macula region has taken place, but in most of the cases seen there is described a white or greyish-white fundus with a small plexus of capillary vessels at the macula region giving a more or less normal red reflex at this

[1] Bibl. No. 251, pp. 377—8. [2] See Fig. 274, *Description of Pedigree Plates*, also Bibl. 299.
[3] Bibl. No. 242. [4] Fig. 272. [5] Fig. 280. [6] Fig. 275.
[7] Bibl. Nos. 121, 187, 210, 234, 316, 325. [8] Fig. 282.

Fig. i

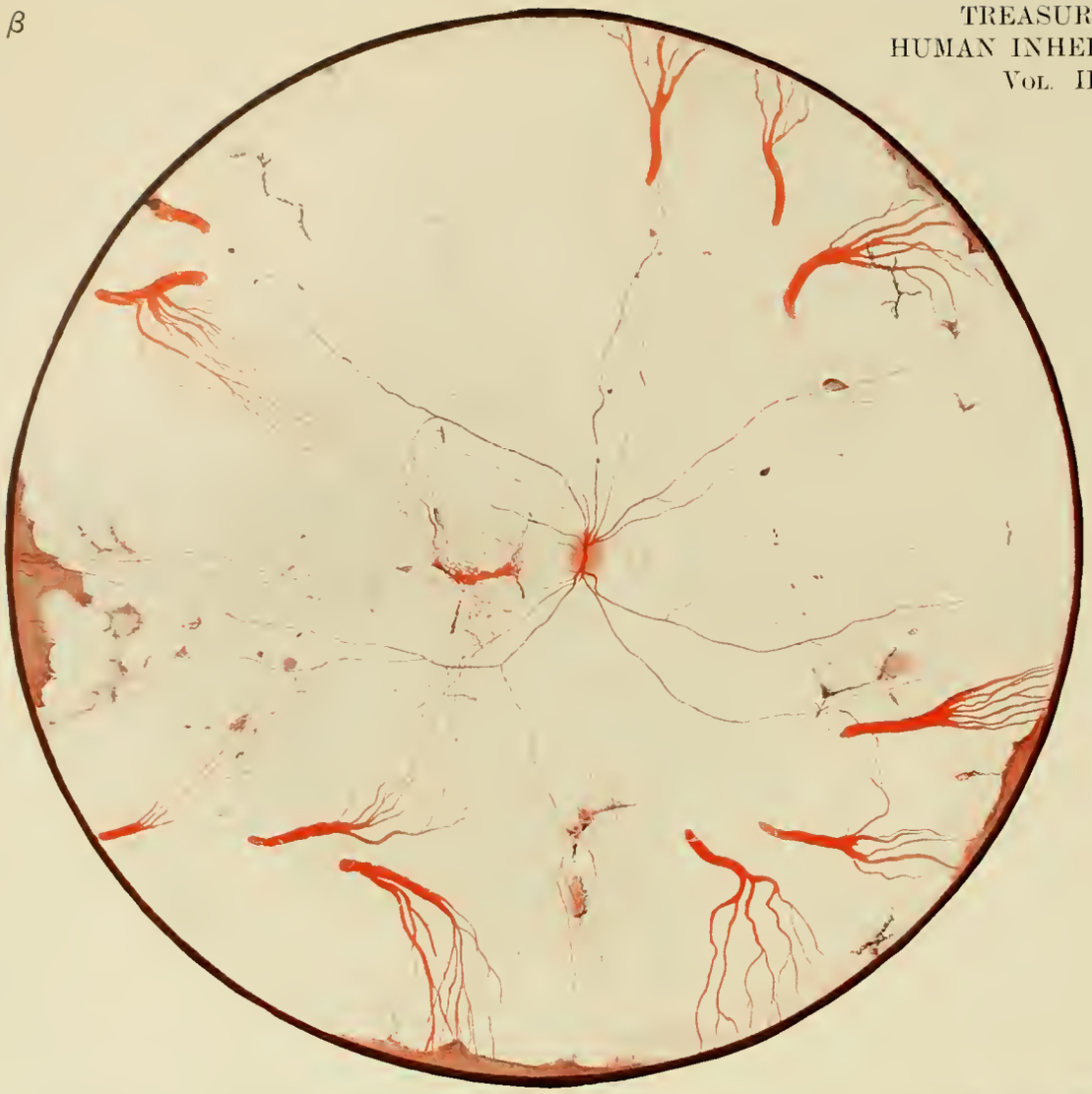

Fig. ii

...in some cases also patches of normal red fundus at the outermost periphery have been noted. Such cases may be [illegible] an arrest in development at a slightly later stage. The beautiful coloured plate which we owe to Usher admirably illustrates all the features of the condition.

Choroideremia is very rare and no anatomical examination of the condition has been made, but the occurrence of the anomaly in Smith and Usher's pedigree[1] in a boy and his mother and sister but not in pigmentosa and whose father had congenital night-blindness, also its occurrence with atypical retinitis pigmentosa and possibly gyrate atrophy of the choroid and retina in Zorn's pedigree[2] suggest that it forms some connecting link in the etiology of these conditions. Zorn's case is of special interest as the patient [illegible] had seven children of whom six were normal and one had possibly *retinitis pigmentosa sine pigmento*.

The defect has been noted in two brothers by Koenig[3], Alexander[4] and Mauthner[5]; Fuchs and others have described cases where siblings or other relatives were reported to be night-blind but had not been examined. It is perhaps worth drawing attention to the fact that all recorded cases in the family had been in males. Other characteristics of the condition are night-blindness which the patient usually reports to have been present since his earliest recollection, the visual fields are contracted; the central vision in a good light may be [illegible] or may be defective; the discs and retinal vessels may be normal but are not [illegible] the condition appears to be either stationary or to progress very slowly. Figures, small pedigrees showing this condition in one or more of the members are given [illegible] Figs. 119, 253, 255, 258—263, 286 and 288.

Gyrate atrophy of the choroid and retina. This condition, which is of extreme rarity was named by Fuchs [illegible] the striking characteristic consists in the appearance of the fundus which [illegible] gave rise to the name of the defect and which shows an irregular zone of choroidal atrophy surrounding the disc, followed by a zone of normal choroid which again is surrounded by a zone of atrophy, the peripheral choroid being normal. The margins of the atrophic zones may be pigmented and are lobulated to form bays which encroach upon the areas of normal choroid. The condition varies much from case to case and of the three sisters, patients of Fuchs and described by Cutler[6] one [illegible] showed a marked divergence from the type that had the condition not been seen in the sisters she would assuredly not have been placed in this group. Other characteristics of the defect are night-blindness, defective vision, contraction of visual fields and [illegible] retinal vessels which may be normal or may be found in retinitis pigmentosa.

The condition has been noted in siblings of either sex, and in one small pedigree[7] a father and son have a defect described by Nettleship in this group though it is in some respects atypical.

[1] See Plate B. [2] Fig. 114. [3] Fig. 262. [4] Fig. 260.
[5] Fig. 255. [6] Fig. 284. [7] Figs. 258, 259, 261.
[8] See also Bibl. Nos. 134, 170, 237, 299, 319 for descriptions of further isolated cases.
[9] Bibl. No. 187. [10] Fig. 263. [11] Fig. 268.

Fig. i. Choroideræmia in a male aged 24 years. Ophthalmoscopic appearance of the right *fundus oculi*; whole *fundus* × *circa* 3.

Fig. i

Right Fundus

Nasal

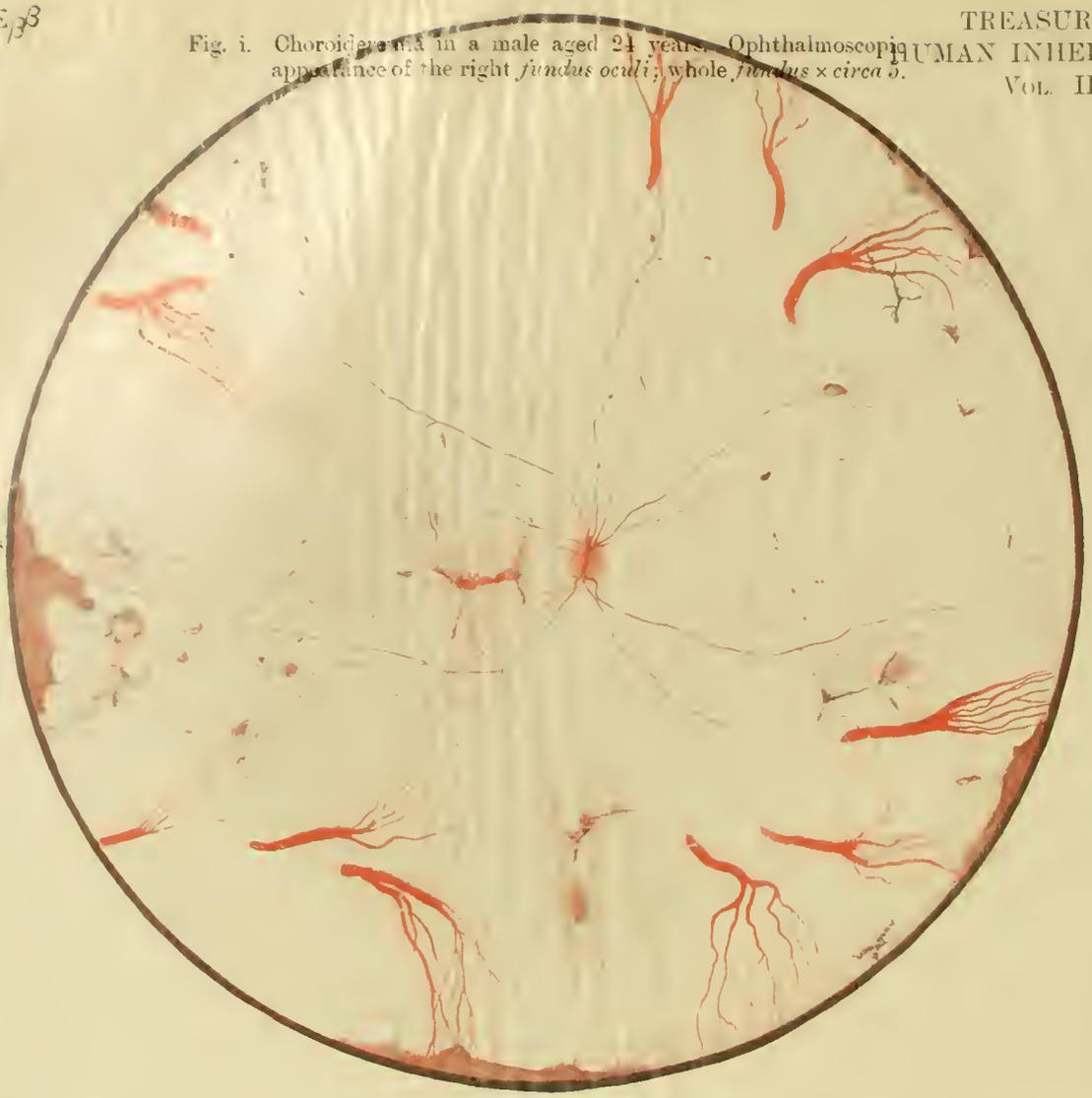

Fig. ii

Fig. ii. Ophthalmoscopic appearance of the left *fundus oculi* of same case; part of *fundus* only × *circa* 8.

lus

Temporal

point, in some cases also patches of normal red fundus at the outermost periphery have been noted. Such cases possibly indicate an arrest in development at a slightly later date. The beautiful coloured plate[1] which we owe to Usher admirably illustrates all the features of the condition.

Choroideremia is very rare and no anatomical examination of the condition has been made, but the occurrence of the anomaly in Smith and Usher's pedigree[2] in a boy whose mother and sister had retinitis pigmentosa and whose father had congenital stationary night-blindness, also its occurrence with atypical retinitis pigmentosa and with possibly gyrate atrophy of the choroid and retina in Zorn's pedigree[3] suggest that there is some common factor in the etiology of these conditions. Zorn's case is of special interest as the patient was married and had seven children of whom six were normal and one had possibly *retinitis pigmentosa sine pigmento.*

The defect has been noted in two brothers by Koenig[4], Alexander[5] and Mauthner[6]; Oguchi[7] and others have described cases whose siblings or other relatives were reported to be night-blind but had not been examined. It is perhaps worth drawing attention to the fact that all undoubted cases so far described have been in males. Other characteristics of the condition are night-blindness which the patient usually reports to have been present since his earliest recollections; the visual fields are contracted; the central vision in a good light may be full or may be defective; the discs and retinal vessels may be normal but are not invariably so; the condition appears to be either stationary or to progress very slowly. Eleven small pedigrees showing this condition in one or more of the members are given below in Figs. 119, 253, 255, 258—263, 286 and 287[8].

Gyrate atrophy of the choroid and retina. This condition which is of extreme rarity was named by Fuchs in 1895[9]; its distinguishing characteristic consists in the appearance of the fundus which in its typical form gave rise to the name of the defect and which shows an irregular zone of choroidal atrophy surrounding the disc, followed by a zone of normal choroid which is again surrounded by a zone of atrophy, the peripheral choroid being normal; the margins of the atrophic zones may be pigmented and are lobulated to form bays which encroach upon the areas of normal choroid. The condition varies much from case to case, and of the three sisters, patients of Fuchs and described by Cutler[10], one of them showed such marked divergence from the type that had the condition not been seen in her sisters she would assuredly not have been placed in this group. Other characteristics of the defect are night-blindness, defective vision, contraction of visual fields and discs and retinal vessels which may be normal or may be as found in retinitis pigmentosa.

The condition has been noted in siblings of either sex, and in one small pedigree[11] a father and son have a defect placed by Nettleship in this group though it is in some respects atypical.

[1] See Plate B. [2] Fig. 119. [3] Fig. 262. [4] Fig. 260.
[5] Fig. 255. [6] Fig. 287. [7] Figs. 258, 259, 261.
[8] See also Bibl. Nos. 134, 170, 237, 290, 319 for descriptions of further isolated cases.
[9] Bibl. No. 187. [10] Fig. 266. [11] Fig. 268.

The condition has not been found in association with retinitis pigmentosa unless we may include the doubtful case described in Zorn's pedigree[1], and although we should like to be able to describe it as due to an arrest in development of the choroid taking place at a later stage than the interruption which occurs in the case of choroideremia we are not able to do so at present. We hope shortly in cooperation with the embryologist to set going some developmental experiments which may throw some light on this question.

Pedigrees which are of interest in this connection may be seen in Figs. 262, 264—268, and 285[2].

[1] See Fig. 262.

[2] See also Bibl. Nos. 187, 188, 209, 297, 317 for references to single cases.

SECTION II

CONGENITAL STATIONARY NIGHT-BLINDNESS

This section is included here for convenience of issue and not out of consideration for any supposed association with retinitis pigmentosa; the two conditions differ fundamentally and the only factors common to both of them are a hereditary disposition and the presence of night-blindness, which is in this case always congenital and stationary, is associated with no visible changes in the fundus and with no other defect of vision except that due to myopia in the sub-group in which it occurs.

The first definite description of the defect as a clinical entity and distinct from the other hereditary diseases in which night-blindness is a marked feature, we owe to Leber who gave a very brief account of the condition in 1877, though several pedigrees of the condition had been published before that date. The earliest recorded hereditary case was, with the possible exception of the single sibship described by Richter[1] in 1830, the famous Cunier pedigree of the Nougaret family published in 1838; it was not however until Nettleship renewed interest in this family and the nature of the case was investigated with the aid of the ophthalmoscope that the Cunier pedigree greatly extended and brought up to date could in 1907 be definitely placed in this group[2]. The condition is of great rarity and only gradually the fact became recognised that the cases classed in this group were not homogeneous but that two definite sub-groups must be formed in one of which should be placed pedigrees in which both sexes are affected and the defect is transmitted by affected members of either sex only, or in some stocks by normal members also, in the second sub-group should be placed pedigrees in which the condition affects males only[3] and is transmitted characteristically by the unaffected female but in a few stocks is also transmitted by the affected male. This second sub-group is further differentiated by the very frequent association of myopia in the night-blind members and occasionally in their 'normal' siblings.

We have then an example of the type of inheritance which follows what is sometimes described as Nasse's[4] law and is seen to hold for such a variety of conditions as haemophilia, pseudo-hypertrophic muscular paralysis, nystagmus, Leber's disease, megalocornea, colour blindness, etc., we can find no common factor in these conditions

[1] See Fig. 297. [2] See Fig. 317.

[3] We obviously cannot be assured in all cases that a small pedigree in which males only are affected should be placed in this sub-group, as more complete information might reveal the defect in females also.

[4] Nasse described this type of inheritance for the case of haemophilia in 1820; he held the view that the male bleeder was in all cases ultimately responsible for the transmission of the disease in a latent form to his unaffected female descendants who were rendered in this way liable to transmit the defect; Lossen however in 1877 as the result of his analysis of the Mampel family (a historic bleeder family) concluded on the contrary that haemophilia was never transmitted through the male bleeder, that his children were only affected if he himself married a conductor and that in all cases it was through the unaffected female that the defect was inherited.

which might offer any clue to the explanation of their common mode of descent; it is significant that sex-limited inheritance should invariably confine the defect to the male and that there is no single hereditary disease known to us in which the female alone is affected.

There has been no advance in our knowledge of congenital stationary night-blindness since Nettleship gave a very complete account of all the available material in 1908. Doubtless owing to the rarity of the defect only two additional good, fully worked out pedigrees have been published since and the more extensive of these we owe to Nettleship. We are still in complete ignorance of the pathology of both types of the defect and cannot even be sure that the seat of the defect is in the eye at all; it has not yet been found possible to make a microscopic examination of the condition.

The defect is not a very serious handicap to the victims, but they are liable to difficulties and accidents which are so well expressed in a letter to Nettleship by one of his patients whom he describes as "a gentleman of scientific tastes and an acute and very trustworthy observer" that we are tempted to quote him fully. He writes: "I have a hand moving in front when in any doubt as to surroundings, and when out alone at night I invariably look up to catch the outline of trees, etc. against the sky unless the latter to me is absolutely black. In what is to me complete darkness I can, without a stick, get along fairly well by feeling the contour of the road or the junction of the roadway and grass. Naturally I have often come to grief when out alone at night, e.g. I three times walked into the canal near my father's house, twice in consequence of thinking a certain light was from one lamp when it was from another, and the third time because I had gone a little further than I thought. Again, I have walked over a wall and fallen six feet into a sunk road; once when walking fast through a village at twilight I cut my face open against a lamp-post, and as a boy I have run into many wheelbarrows and iron railings, and even a horse and cart standing still. At the same time I have never run into a wall or a tree of any size; I always detect the proximity of such a large solid object, sometimes by heat radiating from it, sometimes by a change in the air currents, but much more often by sound—the echo of my own footsteps. I can see very few of the stars, I think only the first magnitude, and though I can manage to get about in gas-lit streets I do not like doing so unless the ground is wet, and I can then see the reflections of the people and vehicles I meet..... I remember once, when I was a boy, being out with friends near the sea, in the daytime, when a thick fog came on, and as we hurried along through a grass field I suddenly stopped and called out; we all listened, and heard the sea breaking below us, the edge of a cliff which we thought a quarter of a mile off being a yard in front of us; I think it was an air current I felt as the sea was very calm[1]."

The disability in this case was evidently of an average intensity, but it is quite clear from other accounts that the defect is a graduated one and that possibly the rarity of published cases should not be taken as an indication of the rarity of the condition but rather as suggesting that the less severe cases are not detected. A correspondent of academic culture wrote to Professor Pearson as follows: "My mother is

[1] Bibl. No. 251, pp. 395—6.

rather myopic and suffers to a certain extent from night-blindness; but neither affection is very strongly marked. Of my eight brothers and sisters the five eldest (girls) give this result: A. (now dead) had normal sight, neither myopic nor night-blind; B. has also normal sight; C. is markedly myopic and is rather night-blind; D. has normal sight; E. is rather myopic, but not night-blind. The next child is myself; I am extremely myopic and perfectly night-blind. My next brother has normal sight; my youngest sister is extremely myopic and is perfectly night-blind; my youngest brother is very slightly myopic, but not at all night-blind." This example clearly indicates the variability of the defect within the sibship and suggests the need for an estimation of the light sense in all the affected and in a large sample of the general population. There are difficulties in the collection of such observations as require 10—20 minutes in a dark room before the test can be made but we hope shortly to find a sufficient number of people willing to come and sacrifice that amount of time and so enable us to get some accurate knowledge of the average light sense and its variability in the general population. We have in our series 33 pedigrees of congenital stationary night-blindness and of these 19 belong to the sub-group in which males and females are affected, 14 to the sub-group in which males only are affected; these numbers are very small but some of the pedigrees are so extensive that the material is not so meagre as might appear. Nowhere do we realise our debt to Nettleship more keenly than here; if we omitted the pedigrees which he worked out or which were investigated owing to his enquiry we should indeed find ourselves with scanty information.

Considering first the sub-group in which both sexes are affected, we find that the sexes are very nearly equally liable to the defect and there is no significant difference in the frequency with which either sex transmits the condition. When we come to examine the proportions of affected and unaffected in the sibships we have at once to admit that the material is entirely overruled by the very extensive Cunier pedigree and Nettleship had some doubts about the accuracy of the numbers given in it; he points out that there was no note of those who died in infancy and that there was a well recognised desire on the part of the family to hide the defect, the mothers fearing that a knowledge of the condition might hamper their children in life and the women fearing lest such knowledge should be a bar to their marriage. There is probably some underestimation of the numbers affected, from these causes, but the mothers were able at a very early infancy to discover whether their children were affected or not, and considering the years of labour devoted to the elaboration of this pedigree in 1838 as well as at the later period by the most indefatigable and careful workers we think that the figures given may be taken as a fairly close approximation to what has occurred; we know well how a whisper of an attempt to hide knowledge of this kind on the part of those giving the information rouses the alarm of the careful worker and tends perhaps too readily to plunge him into doubt and mistrust of the whole family history. Nevertheless the warning must be remembered in any consideration of the figures to be given.

Taking first the affected population only we find that 16·7 % of the individuals have a history of consanguinity in their parents or grandparents; this percentage is considerably lower than that found for retinitis pigmentosa but it is high and indicates

again that consanguinity is a factor of some importance in the etiology of this condition; but as we shall see later we find ourselves again confronted with the position that though we have this high percentage of consanguinity in the stocks in which the defect occurs we do not find a higher percentage of affected members in the offspring of consanguineous parents than in the offspring of unrelated parentage.

Analysing our material and dividing those who were stillborn or died in infancy in the proportion of the affected and normal for the population obtained by omitting sibships in which such cases occur, we get the following table:

	No. of Sibships	No. of Individuals	Percentage affected
Both parents normal ...	11*	71	$43{\cdot}7 \pm 4{\cdot}0$
No Consanguinity			
One parent affected ...	96	357	$41{\cdot}5 \pm 1{\cdot}8$
Mother affected	52	189	$43{\cdot}4 \pm 2{\cdot}4$
Father affected	44	168	$38{\cdot}7 \pm 2{\cdot}5$

* Two sibships were the offspring of first cousins.

Further we find 18 sibships, with one parent affected and a history of consanguinity, consisting of 89 individuals of whom $32{\cdot}6 \pm 3{\cdot}2$ % are affected. Now taking note of the probable errors there is no significant difference in any of the percentages given and indeed all we feel able to insist upon is that a history of consanguinity does not at any rate increase the percentage of affected offspring and that the percentage of affected offspring is probably no greater when one parent is affected than it is for the case of both parents normal[1].

We may add that there is one sibship only in our series for which both parents were affected, they were also distant cousins; this marriage resulted in two children who were both night-blind.

For the sub-group in which males only are affected and the condition is associated with myopia and is transmitted characteristically through the unaffected female but also in certain stocks may be handed on by the affected male, our material is scanty but we notice at once that consanguinity in parentage is no more frequent in this group than it is found to be in the general population and that indeed only 5 % of our affected population have a consanguineous parentage, we may therefore feel assured that consanguinity is of no significance as a factor in the etiology of this type of congenital stationary night-blindness.

Omitting all sibships containing individuals of unknown sex and making the usual allowance for those who died in early infancy we find ourselves with 60 sibships containing 112 affected males, 48 unaffected males and 119 unaffected females. Two interesting facts can be deduced from these figures: (i) The percentage of males affected

[1] When one parent is affected sibships occur in which all are normal, the figures given are therefore not really comparable with those for the case in which both parents are normal.

is very high, no fewer than 70 % of them showing the defect. (ii) There is an excess of males in the affected sibships, as if nature were trying to compensate for their defect by increasing their number, for 57·3 % of the members of affected sibships are males giving an excess of 15 males in every hundred of the population; Bulloch points to a similar excess of males in the affected sibships of the pedigrees of haemophilia. We must point out however that the population of such sibships is not a random sample of the general population with regard to sex but is highly selected in as far as no sibships can be included in which females only occur, affected males have a greater chance of occurring in sibships containing a large number of males than in sibships consisting chiefly of females, sibships with several affected males have a greater chance of record than those with few, and sibships in which all the males are normal are also excluded. With regard to the number of females who transmit the condition the only fact we can really insist upon is the inadequacy of our material; for a large number of unaffected females no statement as to whether they had or had not offspring is made, in other cases they had daughters only and we cannot say whether their sons if they had been born would have been affected or not; such figures as we have indicate that an exceedingly high percentage of the daughters of affected males transmit the defect and that a lower percentage of the daughters of unaffected females (who are nearly always siblings to affected males) hand on the defect to their sons. Thus we find for the daughters of affected males 24 who transmit the defect and only 4 who have unaffected male offspring; this gives a percentage of 86·2 who transmit the defect but we feel convinced that if we had complete information about the large number of cases in which we have no knowledge this percentage would be reduced, perhaps markedly. Again, for the daughters of unaffected females we find 26 who transmit the defect and 13 whose male offspring is unaffected giving a percentage of 66·7 who transmit the defect, a percentage which would again be probably markedly reduced with complete information.

We hope in a future number of this publication to give comparative values for the percentage of affected males in other sex-limited inheritable diseases.

SECTION III

BIBLIOGRAPHY

This Bibliography does not claim to be a complete record of all the literature which has been published on the subject of retinitis pigmentosa and allied diseases; it contains a few references to the early accounts of night-blindness in the chronological order of the authors, and as far as possible all papers of interest from the point of view of heredity. Accounts of isolated cases which give no information of the family history have only been included if they present some special point of interest or have been referred to in the text.

* indicates that the original publication has not been seen.

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104 Vieusse. Une nouvelle forme d'héméralopie, dite "héméralopie temporaire congénitale." *Gazette Hebdomadaire de Médecine et de Chirurgie.* Sér. II., T. XV., pp. 667—669. Paris, 1878. See Fig. 315.

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121 Landesberg, M. Zur Retinitis punctata albescens. *Centralblatt f. praktische Augenheilkunde.* Bd. VII., S. 261—267. Leipzig, 1883. [Three cases described, no family histories given.]

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163 Schmidt, E. Ueber Retinitis pigmentosa. Pp. 3—48. Inaugural Dissertation. Bonn, 1890. See Figs. 14, 132, 220, 235.

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193 Goldzieher, W. Ein Fall von Retinitis pigmentosa mit Glaucoma. *Centralblatt f. praktische Augenheilkunde.* Bd. XXI., S. 116—118. Leipzig, 1897. See Fig. 251.

194 Gould, G. M. Retinitis pigmentosa without the characteristic pigmentation. A report of two cases. *Annals of Ophthalmology.* Vol. VI., pp. 695—710. St Louis, 1897. See Fig. 59.

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201 Schön. Die Ursache der Retinitis pigmentosa. *Centralblatt f. praktische Augenheilkunde.* Bd. XXII., S. 15—18. Leipzig, 1898. See Fig. 13.

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SECTION IV

DESCRIPTIONS OF PEDIGREE PLATES

Pedigree 1 A. *Nettleship's Case.* An extensive family history showing lamellar cataract, "Coppock" or discoid cataract and retinitis pigmentosa in different members of the same pedigree of six generations. See[1] *Treasury of Human Inheritance*, Vol. I., pp. 147—151, Plate XXXII., Fig. 342.

Plate I, Fig. 1 B. *Nettleship's Case.* Thirty-nine individuals affected with retinitis pigmentosa in seven generations. This family was under observation by Nettleship over a period of 24 years, 1883—1907, during which time he examined, in some cases repeatedly, seventeen members. He describes the history as follows: "Descent of the disease in this family was invariably continuous, no healthy pair ever having an affected child. The disease was transmitted by the father six times, by the mother eleven times.

"Not a single case of deaf-mutism, mental defect, or other degeneracy has occurred in this genealogy. The members have been occupied in various small trades or as artisans, and the ones I have seen were above the average of their class in intelligence. They are decidedly long lived.

"The now living head of the family, George Young, IV. 35 aged 66 (1905), has been blind from retinitis pigmentosa for many years....I saw him first in 1883 and 1884 when he was aged 44; the R. eye had then been blind for three years and presented a complete over-ripe cataract, the L. fundus was visible in spite of posterior cortical cataract, and showed extreme retinitis pigmentosa, there was still a little sight in this eye. He said he could not remember ever having seen well at night and believed his day vision had never been so good as that of other people, but he could see to go about easily by daylight till he was aged about 36 years. He was the fourth born of seven children, only one other, IV. 38, lived to grow up, he had good sight and died aged 36 of typhoid fever. IV. 34 and IV. 37 all died in infancy...IV. 35 had five children, V. 49—53 of whom two are normal, one died aged 16 months, and two boys have the family disease...V. 50 aged 11 (1883) had in each eye my. 6 D. and corrected V. $= \frac{2}{10}$ and J. 1; he had a fair complexion, hair straw-coloured; no retinal pigmentation visible by indirect examination but by direct method at periphery a few grains of pigment in the retina and along one or two retinal veins; haze of retina at periphery, choroid at same part was dappled with palish spots; there was a slight loss of upper part of each field. In 1905 I saw him again with hair nearly black, irides brown, very abundant retinitis pigmentosa and posterior polar cataracts.

"V. 52 aged 5 (1884) had V. $= \frac{20}{100}$, improved to $\frac{20}{10}$ by -1 D.; media and optic discs normal; choroid at equator showed round pale dots; some dots and lines of pigment in retina at inner periphery; a patch of complete atrophy of choroid at outer periphery in R. eye. In 1905 he had typical and abundant retinitis pigmentosa, he could still read and write but not easily. V. 49 aged 34 (1905) was examined and found to be normal....Their mother, IV. 36 aged about 65, told me that she used to know which of her children were affected almost when they were in arms, and that by the time they were about four years old the defect was evident enough; she considered that V. 53, who died aged 16 months, was unaffected.

"The others of this genealogy that I have examined are V. 26 and four of her five living children, VI. 30—36, all characteristically affected in different degrees; VI. 35 has been night-blind all her life; VI. 36 aged 22 has severe changes and has been night-blind as long as he can remember; VI. 30 aged $17\frac{1}{2}$ shows decided shrinking of retinal arteries and waxy haze of discs, he is distinctly night-blind according to the testimony of his friends, though he himself is reluctant to admit it. Note that this lad, VI. 30, slightly affected, is the issue of his mother's second marriage, the husband not being her cousin, whilst VI. 35 and 36 by her first husband, who was her cousin and of the affected stock, are both badly affected and have been night-blind as long as they can remember. VI. 22 aged 14 has dappling of choroid at periphery, slight typical pigmentation of retina and shrunken arteries, he cannot remember ever having seen well at night. V. 18 aged 35 had advanced typical changes. VI. 38 was examined, and the three children of V. 45 of whom the eldest, VI. 45 aged 20, has advanced changes, but can still read and sew well; she has about 9 D. of myopia.

"IV. 2 was seen by Mr Hutchinson at the age of 49 in 1869; he had been failing from boyhood but could then still read large letters and see to do his work; he died aged 86 in 1903.

"IV. 35 knows that his mother III. 12, who died aged 70 in 1876 having been blind for twenty years, two of her sisters III. 7 and 9 and her brother III. 1 were all night-blind and became quite blind. From these sources and from IV. 2 he learnt further that his mother's mother II. 2 and her mother I. 1 had the same complaint. III. 1, a local preacher in the Isle of Wight, lived to be 90 and died about the year 1876.

[1] No pedigree published in Vol. I. of the *Treasury of Human Inheritance* will be repeated in Vol. II.

"I have been able to examine III. 20, now aged 90 (1906), hale and active and with perfect eyes; his father, II. 5, had good sight so far as is known, he was a pilot and was drowned, aged 50 years, about 1817. II. 3, died aged 70, was blind for some years before her death but had good sight until she was well advanced in years.

"III. 14, who had only one child, died aged 40 (1855); IV. 25—33 all grew up and married; IV. 8—18 all grew up and their history is well known, none are affected; V. 19—21 consisted of nine children of whom the six eldest grew up and had good sight, the three youngest died in infancy, it is known that none of their children were affected." Consanguinity. Bibl. No. 251, pp. 7—10.

Fig. 2. *Webster's Case.* A girl aged 16 complaining of night-blindness was found to have retinitis pigmentosa with partial atrophy of the optic nerves; she had slight posterior polar cataract in the right lens; her defect had been noticed about the age of 10 years. Her parents were first cousins; her mother, I. 2, had had "weak eyes always." Consanguinity. Bibl. No. 105.

Fig. 3. *Snell's Case.* Twenty-nine cases of retinitis pigmentosa in five generations; night-blindness in all cases appears to have been present in early childhood or infancy; at about the age of 40 those affected became practically blind. IV. 10, aged 46 (1902), had never been able to see well at night, but in the day his eyesight had been fairly good until the last six years when it had rapidly become worse; for two years or more he had been altogether unable to do his work; R.V. $= \frac{2}{60}$, L.V. $= \frac{1}{60}$; the pigmentation of the retina was marked at the periphery, but did not extend towards the papilla so far as is often seen in such an advanced stage of the disease; the discs were white and waxy; in each eye there was a posterior polar opacity of the lens; the fields of vision were contracted to fixation point.

IV. 10 was remarkably well acquainted with all branches of the family. IV. 23 and one of his affected daughters were also examined; in each the condition was typical. No consanguinity. Bibl. No. 227.

Fig. 4. *Schneider's Case.* Retinitis pigmentosa in five generations. The members are described as being healthy and well developed with no sign of hereditary syphilis and no other defect. The ophthalmoscopic appearances of those examined was typical of the disease. I. 1, female, was "born blind" and died in 1852, aged 72. Of her three children, II. 2, a daughter, was night-blind from youth, totally blind at the age of 40 and died aged 65; II. 3, a son, was "born blind" and died aged 2 years; and II. 4, a son, became blind "from cold" at the age of 5 and died aged 7 years. III. 1, night-blind from childhood, had typical retinitis pigmentosa and also anterior and posterior polar cataracts; she had eleven children of whom IV. 2, 3 and 6 were normal and living; IV. 8 died aged 8 years with normal sight and five others, IV. 9, died in infancy. IV. 4 and IV. 7 were affected with retinitis pigmentosa. IV. 2 married and had two normal children, V. 1, 2. IV. 4 married and had three children of whom one, V. 4, aged 3 years had retinitis pigmentosa. The author describes the cases living in considerable detail. No consanguinity. Bibl. No. 192.

PLATE II. Fig. 5. *Nettleship's Case.* This pedigree is of interest as showing severe retinitis pigmentosa associated with no serious degree of night-blindness; a large part of the history was worked out by Major Kilkelly, but the author examined a very considerable number of the members. IV. 8, aged 44, was an intelligent man of outdoor habits; he had very good central acuity separated from a broad belt of peripheral vision by an incomplete ring scotoma which became much larger in a subdued light; he said that he never had difficulty at night, but a relation reported that she had thought for many years that he had some degree of the family blindness; his disease was severe as regards pigmentation of the retina. III. 14, aged 78, mother of IV. 8, had advanced retinitis pigmentosa with some haze of her lenses, but she could see to read until two or three years ago; she had never had difficulty in going about at night; she had lost several fingers of both hands from senile gangrene.

The disease was characterised in this family by its very slow progress and late maturity. No consanguinity. Bibl. No. 251, p. 360.

Fig. 6. *Bordley's Case.* Progressive night-blindness without retinal pigmentation, with symmetrical scotoma in temporal part of field, in five generations. This is a pedigree of great interest and, if it may be classed amongst the cases here being dealt with, is unique in several respects.

The condition is unusually dominant, for thirty-five of the forty-two descendants of I. 1 were known to be affected. The condition in the affected members is characterised by night-blindness, they all had to cease work when the sun set and artificial light only aided them if they were in its direct glare; their vision in good daylight was practically normal in their youth, though one man was myopic (2 D.). The fields of vision were examined for seven members of different branches of the family at different ages, in every case there was a complete loss of the outer lower quadrant of both fields, these scotomata were absolute and did not encroach upon the central portion of the fields; as the light was diminished the fields rapidly contracted until they were reduced to a small central area, for form only; as age increased the fields progressively contracted until the patient became totally blind, and shortly after this death occurred, not one case had lived longer than 16 months after becoming blind. After blindness had developed, the corneae ulcerated and the eyes became infected and were lost; in a case seen by the author, III. 6, there was found to be a loss of epithelium of the left cornea associated with complete anaesthesia of the cornea and the portion of that side of the face supplied by Trigeminus; later the right side became similarly affected and death from apoplexy occurred less than six months after the onset of blindness.

No strabismus or nystagmus were present.

Ophthalmoscopic examination revealed nothing abnormal in the very young children, but showed a very pronounced arterio-sclerosis in older members of the family; except for these rather early vascular changes, the fundi of all examined were perfectly normal, the papillae were normal, and the retinae were free from pigmentary disturbances.

The temporal arteries of even the children were very marked, and the radials were said to be quite stiff. The blood and urine were normal in all cases examined, the blood-pressure was not taken.

This was a negro family; all members were below the normal height, very muscular, intensely ignorant but prodigious workers. It was a misfortune that the author was able to get no record of any member of the family with normal sight having had children. No consanguinity recorded. Bibl. No. 245.

Fig. 7. *Hocquard's Case.* IV. 1, a soldier in an artillery regiment, aged 21 years, was intelligent and robust in general health but he suffered from congenital night-blindness, and was completely blind at night; his colour-sense was normal; his fields of vision were markedly contracted; ophthalmoscopic examination revealed little departure from the normal; there was some infiltration of the retina surrounding the papilla; choroidal vessels could be seen; retinal vessels were almost normal in size, and on the right side there was one oval spot of pigment only, along the trajectory of a vein, on the left side there were two or three grains of pigment of characteristic form present. The father, III. 2 aged 50, an uncle, III. 3 aged 47 years, also a great-uncle, II. 2 aged 79, were all sufferers from congenital retinitis pigmentosa; all other members of the family had excellent sight. No consanguinity. Bibl. Nos. 89, 91.

Fig. 8. *Huidiez' Case.* Retinitis pigmentosa *sine pigmento* in a child aged 8 years who had been under the observation of the author for five years. IV. 1 had very marked night-blindness which had apparently been congenital; visual fields were considerably contracted, central vision was good; some infiltration of the retina was described at the periphery and also surrounding the papilla, but no trace of pigment was visible ophthalmoscopically. Her maternal grandparents were first cousins, and further, a first cousin of the grandmother, aged 55, whose parents also were first cousins, had congenital night-blindness. Consanguinity. Bibl. No. 97.

Fig. 9. *Peltesohn's Case.* II. 2 seen, aged 21, reported that his sight had diminished during the last two years and that it was specially bad at night; he was found to have visual fields which were normal in a good light but were reduced to 10° round the fixation point in a dim light; the retinal vessels were a little narrowed but there was no trace of pigmentation to be seen. He was seen from time to time and the progress of the disease seemed to be rapid, for about three years later his fields were reduced to 5° and he had developed deposits typical of retinitis pigmentosa. He was deaf but was healthy in other respects. The parents were unrelated. His siblings were free from any eye trouble at the time of the first examination of II. 2 but two of them had since then developed night-blindness at about the same age as it appeared in the brother's case. A cousin, aged 30 years, suffered from the same affection. This is interesting as being an undoubted case in which *retinitis pigmentosa sine pigmento* was seen to develop into typical retinitis pigmentosa. No consanguinity. Bibl. No. 158.

Fig. 10. *Cowell's Case.* II. 5 could see well until about the age of 14 years when her sight appeared to fail and she could not see to read at night; soon after this she had scarlet fever, and a year later was unable to read in daylight; she complained of occasional flashes of light and frequent headaches, and when examined her vision was reduced to perception of light and large objects; she had slight nystagmus; the choroid was pale and patchy; the discs were yellowish white with blurred margins; the retinal vessels were small; retinitis pigmentosa was present with a slight amount of pigment only. Her four brothers and her parents were healthy and had good sight. No signs of syphilis were present. No consanguinity. Bibl. No. 111.

Fig. 11. *Maes' Case.* I. 1 and 2 were first cousins with normal eyes; they had six children, five sons and one daughter, of whom two sons, the second and fourth born, had retinitis pigmentosa. II. 2, G. B., was not examined, but it was reported that he suffered from night-blindness, that he had good sight by day, and that his condition was almost stationary; he was unmarried. II. 4, J. B., aged 43 years, suffered from night-blindness, and said that his sight had become worse year by year since the age of 18; he had subjective colour sensations when he was tired; his visual fields were contracted in a dim light; on ophthalmoscopic examination there was found pigmentation of the retina, a slightly atrophic disc, and a semi-transparent film with a few small flecks are described in the vitreous; there were posterior polar cataracts in both eyes. J. B. married and had three sons of whom the two eldest suffered from congenital retinitis pigmentosa. III. 1, E. B., a fair boy, aged 17, had good vision by daylight and had emmetropic eyes but he suffered from night-blindness and his fields were contracted in a dull light; in the retina there was no pigment to be seen but little white specks are described in the equatorial region. The second son, W. B., III. 2, was not examined, but according to the statement of his father he suffered from the same condition to a less severe degree. III. 3 was examined and found to be normal. Consanguinity. Bibl. No. 43.

Fig. 12. *Webster's Case.* Typical retinitis pigmentosa in III. 1. His mother, II. 1, had always seen

badly at night or in a darkened room but had no visible pigment deposits in her retina, she was probably a case of retinitis pigmentosa *sine pigmento*. Parents of III. 1 were first cousins once removed. Consanguinity. Bibl. No. 105.

Fig. 13. *Schön's Case.* Retinitis pigmentosa in a brother and two sisters, also in a daughter of one of the sisters. No information is given of normal members of the family. No consanguinity recorded. Bibl. No. 201.

Fig. 14. *E. Schmidt's Case.* In a sibship of eleven, the offspring of uncle and niece, three members had retinitis pigmentosa, one had kerectasia and the others were said to be myopic. III. 1, aged 21, a female, was said to have typical retinitis pigmentosa. III. 2, a male aged 19, had retinitis pigmentosa with concentric contraction of fields, V. = $\frac{1}{2}\frac{2}{0}$ in each, and also had *ectopia pupillae*. No further information is given. Consanguinity. Bibl. No. 163.

Fig. 15. *Mooren's Case.* II. 1 seen by the author when aged 3 years, had night-blindness and retinitis pigmentosa; he was seen again three years later when the amount of pigment did not appear to have increased but the night-blindness was worse; his mother's sister had five children who were not seen by the author but who were all reported to have either retinitis pigmentosa or congenital night-blindness. No consanguinity. Bibl. No. 114.

Fig. 16. *Gebb's Case.* Two first cousins, who were healthy and whose siblings and ancestors were as far as was known free from any history of inheritable eye disease or disease of the central nervous system, married and had three children II. 1—3. II. 1, a boy aged 6, was healthy but had seen very badly since birth, especially in the twilight; on examination of his eyes it was found that the media were clear; there was a medium degree of myopic astigmatism; the fundus was extremely pale, and the choroidal vessels could be clearly seen as in the case of albinism; the papilla was yellowish red in colour; the retinal vessels were markedly narrowed, especially the arteries which were thread-like; in the macula region were four small delicate pigment deposits, and there were also spots of pigment, not of the 'bone corpuscle' type, in the periphery, the rest of the fundus was absolutely free from pigment. II. 2, aged 4, had seen very badly since birth and was night-blind: he was a healthy boy, and was found to have a medium degree of myopic astigmatism; V. = $\frac{1}{36}$ not improved by glasses; the papilla was pale, the retinal vessels diminished, and there was no trace of pigmentation of the retina to be seen; colour sense was normal. II. 3, a sister aged 2, had the same condition as II. 2; the retinal vessels were very fine, and there was no trace of pigment to be seen in the retina; her vision was better than that of her brothers. The central nervous system appeared to be normal for all. Consanguinity. Bibl. No. 258.

PLATE III. Fig. 17. *Nettleship's Case.* A single case of retinitis pigmentosa in a pedigree which shows the presence of other degeneracies in the stock. IV. 4, Mary Simcox, aged 36, had typical retinitis pigmentosa; she believed her sight was perfect till after her confinement twelve years before when she was very ill and her vision began to fail; she had posterior polar cataracts and some myopic astigmatism; R. V. = 12 J., L. V. = 18 J.; she had seen muscae and "coloured rings and serpents" for some time; pupils acted well; she was night-blind. She was further very subject to nervous occipital headaches, and for three years had had a constant roaring in her R. ear; she was not deaf, and had never had otorrhoea.

III. 3 died, aged 45, of fits following delirium tremens. IV. 1 had infantile convulsions, "her legs never grew below the knees, and she has never walked." IV. 5 and 7 died in infancy. IV. 9 had frequent fits. IV. 11 died, aged $2\frac{3}{4}$ years, "from insanity after a fright." IV. 12, subject to fits after infancy, died aged 12 years "of inflammation." IV. 14 died aged 25, insane. No consanguinity. Bibl. No. 99.

Fig. 18. *Lawford's Case.* (Taken from Nettleship.) Five cases of retinitis pigmentosa in a large sibship, the offspring of "cousins," and with a history of three first cousin marriages in the maternal ancestry in the direct line. VI. 1 had retinitis pigmentosa. VI. 2 had retinitis pigmentosa and was deaf. VI. 3 had retinitis pigmentosa, was deaf and was also an idiot. VI. 7 had retinitis pigmentosa and was deaf. VI. 8 had retinitis pigmentosa. VI. 9 represents two miscarriages. VI. 10 died, aged 3 years, and was believed to have seen well. There was no known case of blindness or deafness or nerve degeneracy in the ancestors of this sibship. No information was available concerning IV. 3, II. 1, or III. 1 and 2. Consanguinity. Bibl. No. 251, p. 39.

Fig. 19. *Nettleship's Case.* IV. 3 married twice; by his first wife he had one child, V. 5, with retinitis pigmentosa, who married and had two normal children, VI. 1; IV. 3 by his second wife, who was his first cousin, had four children, of whom V. 1 died, aged 6 years, mentally deficient, V. 2 was a miscarriage, V. 3, aged 13, had retinitis pigmentosa and was mentally deficient, V. 4, aged 6, was normal. IV. 1, maternal aunt to this sibship, was mentally defective, and her great aunt and great uncle, II. 1 and 2, were insane. Consanguinity. Bibl. No. 251, pp. 26—7.

Fig. 20. *Nettleship's Case.* Three cases of retinitis pigmentosa in a sibship of nineteen, of whom eleven died young. IV. 2 and 17 died in childbed; IV. 3, 4 and 5 died in infancy; IV. 6, an idiot, died aged 7; IV. 7, aged 40, had retinitis pigmentosa, she was also deaf and was half idiotic; IV. 9 was normal and had normal children; IV. 14, aged 30, was mentally feeble and had retinitis pigmentosa; IV. 15 had retinitis

pigmentosa; IV. 16 died, aged 18, of an accident. The father, III. 4, aged 74, had excellent sight, but nothing was known of his ancestors. The mother, III. 3, aged 70, had six siblings, of whom three were still living; her mother, II. 2, was one of a sibship of twenty-two of whom six died young, one of the survivors, II. 3, had fits. No consanguinity. Bibl. No. 251, pp. 23—4.

Fig. 21. *Nettleship's Case.* Retinitis pigmentosa in two members of a sibship of eleven. III. 1, aged 26, had a slight defect in her sight but was not seen. III. 3, aged 24, had never been able to see well at night, and was getting slowly worse; he had typical retinitis pigmentosa with scanty pigmentation; changes in the discs and vessels were relatively advanced, choroids were extremely pigmented; refraction normal; he had black hair, brown irides, was well grown and intelligent and was not deaf; he had been married 7 months. III. 6, aged 17, was well grown and intelligent but excitable; she only noticed that she was night-blind about six months ago when she began dress-making; she had typical retinitis pigmentosa with pale slightly hazy discs and much diminished vessels; no opacities in vitreous or lens. III. 7 died, aged 6 years, from "water on the brain," he "had no bones and could not walk unless splintered up to the waist," was intelligent, and head was not very large. III. 8 died, aged 6 months, of "inflammation on the chest." III. 11, aged 8, was described as "very peculiar and excitable, brain too active and head rather large," any little excitement was liable to make him delirious and disturbed at night.

I. 2 was insane in old age. I. 3, half-sister to I. 2, became blind and died paralysed and insane at the age of about 30. II. 2, not examined, was said to be very "short-sighted." II. 7 was said to be half imbecile. II. 8 married her first cousin and had children, of whom some were said to be defective in intellect. There were normal offspring from some members of II. 3—6. Consanguinity. Bibl. No. 99.

Fig. 22. *Nettleship's Case.* Four cases of retinitis pigmentosa in three generations. John Mills, III. 3, aged 57, and his sister, III. 2, aged 70, had the disease, also his mother, II. 1, and his maternal grandmother, I. 1. He probably had more than one sibling. Of his ten children four died in infancy, one son, an idiot, died aged 18, and five were living and normal. No consanguinity. Bibl. No. 251, p. 13.

Fig. 23. *Lawford's Case.* (Taken from Nettleship.) One case of retinitis pigmentosa, IV. 1, and one congenital idiot, IV. 4, in a sibship of four. The parents, III. 1 and 2, were half first cousins; the maternal grandfather, II. 2, and paternal grandmother, II. 3, were half siblings by the same father, I. 2, and different mothers. Consanguinity. Bibl. No. 251, pp. 46, 336.

Fig. 24. *Herrlinger's Cases* 22 *and* 23. Four cases of retinitis pigmentosa associated with deaf-mutism, idiocy and polydactylism. IV. 1, aged 14, had seen badly since childhood, and his vision was now reduced to finger counting; he had retinitis pigmentosa, was an idiot, was deaf, and had six toes on each foot and six fingers on his left hand. IV. 2, aged 12, had retinitis pigmentosa and was an idiot; her vision was reduced to finger counting. IV. 3 was an idiot, had bad sight and had polydactyly; she was not examined. IV. 4 represents four siblings who died young. IV. 5 represents four healthy and normal siblings. IV. 6, son of a paternal uncle to the sibship IV. 1—5, was blind and a deaf-mute.

The parents, III. 1 and 2, were healthy and unrelated. I. 2 was a deaf-mute, I. 3 an idiot. No consanguinity. Bibl. No. 203.

Fig. 25. *Herrlinger's Cases* 3 *and* 91. Retinitis pigmentosa in two brothers whose parents were first cousins on their father's side and second cousins on their mother's side. IV. 1 and 2 died in infancy. IV. 3 was stillborn. IV. 4 and 5 were healthy. IV. 6, aged 7, had seen badly since birth and his vision was now reduced to finger counting, he had retinitis pigmentosa and was mentally defective. IV. 7, aged 4, had retinitis pigmentosa *sine pigmento*, his vision was reduced to perception of light. The parents and other relatives had normal vision. Consanguinity. Bibl. No. 203.

Fig. 26. *Webster's Case.* A healthy man and woman, I. 1 and 2, had two healthy sons, II. 2 and 3. II. 2 married and had five living children of whom two had retinitis pigmentosa and three daughters saw well. III. 1, aged 42, was examined and was found to have the right retina loaded with pigment deposits, the left retina showing the same condition in a less severe stage; there was partial atrophy of the discs; the fields were irregularly contracted with numerous scotomata; her vision had always been poor, but was getting worse.

II. 3 married his first cousin and had nine children of whom three became blind and afterwards idiotic, five were presumably healthy, III. 8 had good sight but died of a "chronic disease of the nervous system." Consanguinity. Bibl. No. 105.

Fig. 27. *Nettleship's Case.* Retinitis pigmentosa in two brothers, III. 1 and 3; they had two normal brothers, III. 2 and 4. The father, II. 2, had had eleven siblings of whom four died of phthisis, one died in infancy and six were living. His father, I. 3, committed suicide; his mother, I. 2, and her sister, I. 1, died of phthisis. No consanguinity. Bibl. No. 251, p. 23.

Fig. 28. *Herrlinger's Case* 90. Retinitis pigmentosa in III. 1, aged 7 years. His sister, III. 2, aged 5, was blind, two brothers, aged 3 and 2 years respectively, saw well. The father and grandfather were drinkers. The maternal grandfather, I. 4, had a congenital defect in his foot. The sister of the maternal grandmother had a daughter who was blind and an idiot. No consanguinity. Bibl. No. 203.

Fig. 29. *Harlan's Case.* Four siblings born blind, or with slight perception of sight only, in a sibship of six. The eldest and youngest were normal. One blind child had died, one was an idiot, and the others were rather deficient in intellect. One case only was examined, he, II. 2, aged 21, had contracted and immovable pupils, and nystagmus; pigmentation of the retina was well-marked in the periphery but not abundant. There was no known hereditary predisposition to retinitis pigmentosa. No consanguinity. Bibl. No. 82.

PLATE IV. Fig. 30. *Nettleship's Case.* One case of retinitis pigmentosa in a pedigree which shows freedom from disease in the direct line for three previous generations on the maternal and two on the paternal side; no information was obtained of the collaterals. The patient, a woman aged 40, had ten normal siblings; she was married and had four normal children. She showed no signs of hereditary syphilis, and there was nothing to suggest acquired syphilis; the eye changes were typical of ordinary retinitis pigmentosa. No consanguinity. Bibl. No. 251, p. 21.

Fig. 31. *Scimemi's Case.* Two normal first cousins, III. 1 and 2, married and had five sons of whom three were normal and two, IV. 2 and 3, had retinitis pigmentosa; IV. 3 married his second cousin, IV. 4, and after a miscarriage they had a daughter, V. 3, who at the age of 26 was seen to have retinitis pigmentosa. After the death of IV. 3, his brother, IV. 2, married the widow, IV. 4, his second cousin; they had a daughter, V. 1, who had a progressive diminution in vision, and was believed to have retinitis pigmentosa, although the characteristic changes in the fundus had not yet appeared at the time of examination. Consanguinity. Bibl. No. 207.

Fig. 32. *Nettleship's Case.* Retinitis pigmentosa with atypical symptoms but typical changes in two sisters, V. 2 and 3, who had two normal sisters; they were the offspring of second cousins. No known history of bad sight in generations I.—IV., but details of generation I. could not be obtained. Consanguinity. Bibl. No. 251, pp. 47, 336.

Fig. 33. *Bayer and Nolden's Case.* I. 1 was described by Bayer when she was aged 42; she had suffered from retinitis pigmentosa for thirty years; she could read Jäg. No. 14, her fields showed concentric contraction, the retinal vessels were not much narrowed, and she had a slight deposit of pigment in the periphery of the retina. She had five children, four or five of whom suffered from night-blindness. Nolden described one of these, a boy, II. 1, Wilhelm Fassbender, aged 10 years, whose vision $= \frac{10}{20}$, his fields were contracted, and the pigmentation of the retina was typical though scanty. No consanguinity. Bibl. Nos. 75, 94.

Fig. 34. *Wider's Case.* Retinitis pigmentosa in three sisters aged 63, 53 and 51 respectively when examined; in each case vision was reduced to hand movements only, all were myopic and had only very small fields of vision; the fundi were typical of the disease. They had one brother who was said to see very badly. The parents were normal and related in the "3rd Grade." There had been much intermarriage in the families, and numerous relatives were said to be blind or to be night-blind. Consanguinity. Bibl. No. 137.

Fig. 35. *Nettleship's Case.* Retinitis pigmentosa with day-blindness and colour-blindness in three members of a sibship of nine, the offspring of first cousins once removed. The affected members were V. 2, aged 34, a woman who was married and had two normal children; V. 7, a male aged 24; V. 8, a male aged 21; V. 6 died, aged 11 years, of "fever." The father, III. 3, died, aged 50, of heart disease; the mother, IV. 1, aged about 57, was melancholic. No information about the maternal grandmother, III. 1. Consanguinity. Bibl. No. 251, p. 45.

Fig. 36. *Dean's Case.* Two sisters marry two brothers, their first cousins; five cases of retinitis pigmentosa occur with two normal members in the resulting sibships. III. 1, aged 17 years, had typical retinitis pigmentosa, his vision was reduced to finger counting only at 1 m. III. 2, aged 15 years, was partially blind. She could not see to count fingers, and her fundus showed typical retinitis pigmentosa. III. 3, aged 9 years, had good vision. III. 4, aged 4 years, was blind. By the second sibship, III. 5, aged 16 years, was almost blind and could not see to count fingers, the fundus again showed typical retinitis pigmentosa. III. 6, aged 13 years, had normal vision. III. 7, aged 10 years, could not see to count fingers, had typical retinitis pigmentosa and further had degenerate changes in his teeth; thus the two upper central incisors were absent and the two lower ones were about one-third the normal size, the two upper lateral incisors were small and conical, the two lower ones were only about a quarter the normal size. Consanguinity. Bibl. No. 211.

Fig. 37. *Rosenbaum's Case.* Retinitis pigmentosa in II. 1, aged 41; V. $= \frac{8}{60}$. An uncle, I. 3, and two brothers, II. 2 and 3, suffered from night-blindness. No consanguinity recorded. Bibl. No. 213.

Fig. 38. *Simi's Case.* Three cases of retinitis pigmentosa in a sibship of five, no other cases being known in the family. Sebastiano Giannini, aged 7, had both eyes affected with retinitis pigmentosa, the deposits being more profuse in the right eye; vision was completely lost; his two brothers were said to be as blind as the patient. Two sisters had excellent sight. No consanguinity. Bibl. No. 60.

Fig. 39. *Trousseau's Case.* Retinitis pigmentosa in IV. 1, aged 12, the illegitimate child of an uncle and

niece. The parents and very aged grandparents were examined and found to have normal eyes; a maternal aunt, III. 2, was examined and was found to be nearly blind with retinitis pigmentosa. Consanguinity. Bibl. No. 171.

Fig. 40. *Nettleship's Case.* I. 1 was blind at the age of 40, probably from retinitis pigmentosa; his son, II. 1, had normal vision, he was married and had several children, of whom one, a daughter, had typical retinitis pigmentosa. No consanguinity. Bibl. No. 251, p. 19.

Fig. 41. *Siegheim's Case.* Retinitis pigmentosa in two siblings and their paternal great-uncle. No information of normal members of the family. No consanguinity recorded. Bibl. No. 146.

Fig. 42. *Snell's Case.* Six cases of retinitis pigmentosa in a sibship of eight. The father, I. 1, aged 56, had normal fundi, hypermetropia 4 D. and V. = $\frac{20}{30}$ in each eye. The mother, I. 2, was myopic, but otherwise her eyes were normal. II. 1, aged 27, was myopic, – 5 D., V. = $\frac{20}{50}$, her fundi were normal. II. 2, aged 25, had always seen badly at night, the disability increasing with his age; the retinal periphery was studded with pigment, the margins of the discs were a little blurred; he was myopic and V. = $\frac{20}{30}$. II. 3, aged 24, was night-blind and had well-marked pigmentary deposits in the retina; R.V. = $\frac{20}{50}$, L.V. = $\frac{20}{70}$, slightly improved by + glasses. II. 4, not examined, was reported to suffer in the same way as his brothers. II. 5, aged 18, was night-blind, and had deposits of pigment scattered round the periphery of the retina; the discs were paler than normal; he had myopia – 4D., and V. = $\frac{20}{50}$; his fields showed concentric contraction. II. 6, aged 17, had seen badly at night for four years; small pigment dots were seen at the periphery of the retina; he had a high degree of myopia and astigmatism. II. 7, aged 14, had always seen badly at night; pigment dots were seen at the periphery of the retina; V. = $\frac{20}{50}$. II. 8, aged 13, was not night-blind, the retina was a little mottled at the periphery, but no deposits of pigment were present; he was hypermetropic, V. = $\frac{20}{20}$.

Careful inquiry could discover no evidence on either parent's side of night-blindness in their progenitors. In all the brothers the complexion was florid and hair was fair; they were all healthy looking market gardeners. No consanguinity. Bibl. No. 147.

Fig. 43. *Gonin's Case.* Th. B., II. 2, aged 30, was the third of twelve siblings; he had had night-blindness since infancy and had typical retinitis pigmentosa; central visual acuity = $\frac{5}{10}$; he had myopia of 2 D.; visual fields were contracted in a lowered light and showed an annular scotoma. A sister aged 20 years had night-blindness; seven living siblings were normal, and three siblings were dead, of whom there was no information. The parents were healthy "cousins of the 8th degree." No ocular affections were known in the antecedents. Consanguinity. Bibl. No. 218.

Fig. 44. *Smyth's Case.* (Taken from Nettleship.) Two cases of retinitis pigmentosa in a sibship of seven. The affected members were a male, the fifth born and a female, the youngest of the sibship. Three brothers were normal, one brother died in infancy, and one female, IV. 6, was normal. The parents, believed to be normal, were uncle and niece. Consanguinity. Bibl. No. 251, p. 34.

Fig. 45. *Rosenbaum's Case* 13. III. 1, aged 19, had retinitis pigmentosa; V. = $\frac{6}{9}$. Her maternal grandfather, I. 1, her mother, II. 2, all her mother's siblings (number not given) and two of her three siblings were night-blind. No consanguinity recorded. Bibl. No. 213.

Fig. 46. *Ayres' Case.* In a sibship of seven, four boys have such defective sight that they are unable to plough a field or drive a reaper, and one girl also has defective sight; the first and fifth born, two girls, have good sight. Only one case was examined; he, aged 25 years, had typical retinitis pigmentosa with greatly contracted fields and with vision so imperfect that he was unfit for ordinary work. The parents were cousins and the mother delicate. Consanguinity. Bibl. No. 138.

Fig. 47. *Nettleship's Case.* Nine cases of retinitis pigmentosa in three generations. Two affected sisters, II. 1 and 3, had a normal brother, II. 2. II. 3 married and had seven children of whom three sons and one daughter had retinitis pigmentosa, one son and two daughters were normal. The two normal daughters, III. 2 and 4, had each a normal child. One affected son, III. 7, was believed to have five normal children. III. 9, an affected son, was known to have an affected daughter, IV. 8. III. 11, the affected daughter was known to have two affected sons, IV. 10 and 13, and four normal children of whom three were daughters. No consanguinity. Bibl. No. 251, pp. 13—14.

Fig. 48. *Frenkel and Dide's Case.* Retinitis pigmentosa associated with severe defects of the central nervous system in three siblings. II. 1 was normal to the age of 7, she talked, walked and was learning to read; in her seventh year her sight diminished, and a year later she was believed to be blind, but she evidently saw still in the day; a little later she became ataxic and later still mental troubles developed; towards the age of 13 convulsive attacks commenced with loss of consciousness, salivation, tonic convulsions and stertor; she died aged 20. II. 7, aged 18, was normal to the age of 8 when her sight diminished; at puberty she became ataxic and later had epileptiform attacks; she had slight convergent strabismus, no nystagmus, pupils reacted, media were transparent; R. fundus showed atrophy of temporal side of disc which was also pale on the nasal side, arteries narrowed, margins of disc clear, and there was typical retinitis pigmentosa; similar conditions were present in the L. fundus, though here the pigmentary deposits

approached nearer to the papilla; visual acuity and fields could not be examined. The authors give a detailed description of the conditions found in the central nervous system. II. 8, aged 13, was normal to the age of 7½ since when her vision had progressively diminished; she had slight convergent strabismus, pupils reacted sluggishly, nystagmus was present, media were transparent, fundi were typical of retinitis pigmentosa.

The parents were both living, there was no history of nervous or degenerative disease or troubles with vision in them or any of their relations, there was no syphilis and no consanguinity. The family was Catholic and of Spanish origin. The first patient was born two years after marriage; II. 2 and 3 were twin boys born three years later who both died aged 6 or 7 days; II. 4, born one year later, was living and well, aged 28, and had a healthy daughter; II. 6, a boy, born two years later, died, aged 2, of meningitis. No consanguinity. Bibl. No. 289.

Fig. 49. *Leber's Case.* Retinitis pigmentosa in two brothers and a sister with three normal siblings; parents and grandparents were normal. III. 1, aged 34 years, had suffered since his twelfth year when he first noticed night-blindness and a rapidly increasing amblyopia; a year later he could only read with difficulty; ophthalmoscopic appearances were typical of the disease, the pigment reaching to the neighbourhood of the papilla. No consanguinity. Bibl. No. 72.

PLATE V. Fig. 50. *Snell's Case.* Twelve cases of retinitis pigmentosa in a pedigree of five generations, generation II. being free from the defect. III. 8, aged 45 (1906), complained of his sight being very defective especially at night; he was found to have severe retinitis pigmentosa with waxy looking discs; R.V. = $\frac{1}{60}$, L.V. = $\frac{4}{60}$; the fields of vision were reduced to a very small area, little more than fixation point. The author also examined IV. 6, aged 12, who was normal, and V. 3 who was affected. No consanguinity. Bibl. No. 244.

Fig. 51. *Herrlinger's Case* 71. Retinitis pigmentosa in a girl, aged 19 years, whose grandmothers were half-sisters by their mother, II. 2, and whose great-grandfathers, II. 1 and 3, were brothers; she also had convergent strabismus. The parents were normal. Consanguinity. Bibl. No. 203.

Fig. 52. *Nettleship's Case.* Nine cases of retinitis pigmentosa in two sibships of the same generation; one grandfather, I. 2, was believed to have had the disease, his wife and their five children were certainly normal. II. 2 had ten children of whom III. 1 aged 28, III. 4 aged 24, and III. 7 aged 10 had retinitis pigmentosa; III. 8 was stillborn, III. 9 died of "croup" in childhood. II. 3 had thirteen children of whom six males had retinitis pigmentosa and their seven siblings had good sight; none of this sibship were examined. II. 5 had several children, one of whom was "near-sighted but not like the night-blind ones," the others were normal. No consanguinity. Bibl. No. 251, p. 20.

Fig. 53. *Gonin's Case.* Victor B., III. 3, aged 18, suffered from retinitis pigmentosa with typical appearance of fundus; V.R. = V.L. = $\frac{1}{10}$; he had myopia of 6 D. in R. and 8 D. in L.; visual fields were contracted. His elder brother, aged 20, suffered from night-blindness; his younger brother was only aged 4 and no information was given of his eyes; his seven sisters had good sight. I. 2, the maternal grandfather, lost his sight gradually about the age of 40 without knowing the cause. II. 3, a maternal aunt, had several children with "weak sight." II. 5, the father, had atrophy of the optic nerve following a retrobulbar abscess four years previously No consanguinity. Bibl. No. 218.

Fig. 54. *Rosenbaum's Case.* Retinitis pigmentosa in III. 3, aged 25 years; R.V. = $\frac{8}{18}$, L.V. = $\frac{8}{12}$; fundus examined. Consanguineous marriages had occurred in the mother's family. A brother, aged 36 years, and a sister, aged 38, also suffered from retinitis pigmentosa. The mother, the maternal grandfather, a maternal uncle and his child all suffered from night-blindness. The author does not refer to any normal members of the family. Consanguinity. Bibl. No. 213.

Fig. 55. *Maes' Case.* Retinitis pigmentosa in two brothers and a sister with six normal siblings; the parents and grandparents were normal. One case only was examined, he, aged 51, had suffered from night-blindness as a child; his vision had become greatly diminished during the last two years; he had normal lenses and discs; the arteries of the retina were somewhat narrowed; the fields were contracted and the retina was pigmented. No consanguinity recorded. Bibl. No. 43.

Fig. 56. *Mooren's Case.* Retinitis pigmentosa in a boy, III. 1, his father and two uncles, and also in his paternal grandmother; the latter was not examined by the author. No consanguinity recorded. Bibl. No. 114.

Fig. 57. *Mooren's Case.* Two first cousins married and had six children of whom two sons had retinitis pigmentosa; one of the normal sons of this sibship married and had four sons of whom one had retinitis pigmentosa, one had congenital night-blindness, and two had normal sight. One of the affected sons of the sibship, II. 3, married his cousin and had four children who all suffered from retinitis pigmentosa. Consanguinity. Bibl. No. 114.

Fig. 58. *Mooren's Case.* Retinitis pigmentosa in a nine year old girl, III. 1, in her father, II. 2, and his three brothers, II. 3, 4 and 5, and in her paternal grandmother, I. 1. Most of these cases were examined

by the author who however makes no reference to any unaffected members of the family. No consanguinity recorded. Bibl. No. 85.

Fig. 59. *Gould's Case.* III. 2, aged 26 years, a typist, complained of headache with obscure ocular and cerebral symptoms apparently due to eye strain. R.V. with −Sph. 0·37 −Cyl. 0·24 ax. 180° = $\frac{2}{20}$, L.V. with −Cyl. 0·37 ax. 180° = $\frac{2}{30}$. Preliminary ophthalmoscopic examination was negative. For 3 years she had had difficulty in walking alone at night, and on examining her fields it was found that for white the fields were contracted to about half the normal, and for colours they were very small and irregular in outline; colour sense was normal; with extreme care the author could now detect numberless obscure tiny dots, brownish or blackish, strewn over the retinal periphery. III. 1, brother to III. 2, aged 29, was also examined and the condition was just as in his sister's case; the retinal vessels and discs were normal in both cases. Two other siblings, a sister and brother, had normal eyes. The parents were normal, but the paternal grandfather was night-blind all his life, and was quite blind at the age of 70. No consanguinity recorded. Bibl. No. 194.

Fig. 60. *Oliver's Case.* Fourteen cases of retinitis pigmentosa in three generations. II. 2 had for many years been unable to see at night, and now had become unable to read by daylight. The ophthalmoscope showed a typical retinitis pigmentosa with almost entire absence of retinal vessels and advanced optic atrophy. All cases were examined except I. 1, II. 7, III. 8 and 9 but no further details were given. There was no knowledge of other cases in the ancestry. No consanguinity recorded. Bibl. No. 294.

Fig. 61. *Herrlinger's Cases* 42, 43. Three cases of retinitis pigmentosa in a sibship of fifteen, of whom ten were dead. The parents were normal and unrelated, the paternal grandparents were first cousins. III. 1, aged 27, had suffered from night-blindness since his school days; V. = finger counting at $\frac{1}{2}$ m.; refraction, myopia of −3 D.; retinitis pigmentosa was found. III. 2, aged 15, was similarly affected; for her R.V. = $\frac{2}{60}$, L.V. = $\frac{4}{60}$: refraction, myopia of −4 D. in R., −3 D. in L. III. 3, aged 13 years, was said to be affected to a less degree than III. 1 and 2. III. 4 and 5 were normal and saw well. Consanguinity. Bibl. No. 203.

Fig. 62. *Harlan's Case.* Retinitis pigmentosa in three siblings, their mother and their maternal grandfather. III. 1, aged 20, had always been night-blind, and was at the time of observation just able to see to go about alone and could recognise persons in bright daylight; blindness was absolute except in the region of the macula. III. 3, aged 16, never had good sight, but could recognise persons up to the age of 10, since when she has had quantitative vision only; she had external strabismus and nystagmus. III. 2, said to be similarly affected, was not examined. Three brothers and three sisters were reported to have had normal vision, two of them however died young. No consanguinity recorded. Bibl. No. 82.

Fig. 63. *Nettleship's Case.* Retinitis pigmentosa in five members of a sibship of eight. The patient, III. 5, aged 26, said that all her sisters, one of her four brothers, her mother and "all" relatives on her mother's side had the disease; three of her brothers had normal vision. The author was unable to get more information concerning the cases in this family. No consanguinity recorded. Bibl. No. 251, p. 16.

Fig. 64. *Mayou's Case.* III. 1, aged 17 years, had suffered from night-blindness for two years; Wassermann test negative. Her fundus showed typical but not very marked retinitis pigmentosa, the discs were slightly grey, retinal vessels almost normal in size, lenses were clear, fields of vision contracted to the ten degree circle, pigmentary deposits in the periphery of the retina. There was some improvement in the fields on paracentesis, and the author therefore trephined; a week later the patient reported that she had lost her night-blindness, and her fields were markedly improved. Her aunt, II. 3, showed far more extensive changes and was practically blind; she also showed marked improvement in her fields after trephining. The author was of the opinion that the improvement was possibly temporary, and this proved to be the case. The patient's father, her grandfather and her brother were also affected. No consanguinity recorded. Bibl. Nos. 305, 309.

Fig. 65. *Ancke's Case.* III. 1, aged 18 years, complained of night-blindness which she had noticed since the age of 7: she had good central vision but her fields were contracted in daylight and much more so in a dull light; fields for colour were much more markedly contracted; her fundus showed a typical retinitis pigmentosa. III. 2, aged 17, had normal vision. III. 3, aged 16, did not suffer from night-blindness, her central vision was good, but the fields were markedly contracted in a dull light; the periphery of the fundus was seen to be stippled with numerous small white spots which were not confluent and further there was seen a typical fine distribution of pigment of the 'bone corpuscle' shape; the arteries were narrowed. III. 4, aged 14, did not complain of his sight but he suffered from night-blindness and was found to have fields full in daylight but contracted in a dull light; retinitis pigmentosa was found on ophthalmoscopic examination. III. 5, aged 12, had normal vision. The parents of this sibship were first cousins. Consanguinity. Bibl. No. 132.

Fig. 66. *Nettleship's Case.* Retinitis pigmentosa in two brothers in a sibship of six. III. 1, 3 and 5 were examined and found to be normal; III. 2, died, aged 1½ years, of measles; III. 4 and III. 6, aged 9, were affected. The maternal grandparents, who both saw well, were "half-cousins." Consanguinity. Bibl. No. 251, p. 43.

Fig. 67. *Nettleship's Case.* Retinitis pigmentosa in a brother and sister who had one normal brother, III. 1, aged 46; the mother, II. 1, and maternal grandmother, I. 1, were also affected. The parents were "distant cousins," the maternal grandparents were "cousins." Consanguinity. Bibl. No. 251, p. 25.

PLATE VI. Fig. 68. *Maes' Case.* Retinitis pigmentosa in three siblings, eight other siblings died young; parents and grandparents were normal and unrelated. III. 1 was seen, aged 56, he reported that he had seen quite well even in the evening up to his eleventh year, but since then his sight had steadily got worse until now in bright daylight his fields of vision were contracted; he had posterior polar cataracts but the pigment of the retina could be seen between them; he was also deaf. III. 1 reported that his two living sisters had the same disease and had become almost blind at about the age of 50; one of the sisters was also deaf. No consanguinity. Bibl. No. 43.

Fig. 69. *Ransohoff's Case.* II. 2, aged 55 years, came up for treatment for hypopyon keratitis of the left eye, she had always been short-sighted and seen badly, but was able to do her own housework. On examining the right eye it was found that the papilla was pale, the vessels narrowed and there was a considerable development of pigment in the periphery of the retina. She had four siblings of whom three could see well, but the youngest sister was short-sighted and night-blind. This sister had five children none of whom had retinal disease, but two of whom had myopia of 6 D. and 9 D. respectively. II. 2 married a healthy man with normal eyes and no history of eye disease in his family; of their seven children four had retinitis pigmentosa and myopia. III. 1, Wilhelmine, had retinitis pigmentosa and myopia of 9 D. III. 2 was normal. III. 3, Gustav, had retinitis pigmentosa, a R. posterior polar cataract and myopia of 5 D. III. 4, Emil, had normal eyes. III. 5, Carl, with retinitis pigmentosa, had myopia of 5 D. III. 6, Wilhelm, had retinitis pigmentosa with myopia of 10 D., and III. 7, Franz, had normal eyes. No consanguinity. Bibl. No. 167.

Fig. 70. *Dean's Case.* Retinitis pigmentosa in a boy, III. 1, aged 13 years, whose fundus showed the typical changes, V. $= \frac{6}{\frac{1}{12}}$; he had one younger brother whose eyes were apparently normal. The mother seen, aged 35 years, had retinitis pigmentosa and also cataract. The maternal grandfather, I. 2, had been blind since the age of 35, and had complained of night-blindness before he became totally blind. No consanguinity recorded. Bibl. No. 211.

Fig. 71. *Maes' Case.* Retinitis pigmentosa in two brothers whose parents and grandparents were normal and unrelated. One only of the brothers was examined, he, III. 2, had had good sight with no difficulty in the evening light up to his 17th year, but since then his vision had slowly diminished; when examined at the age of 40 he had night-blindness, contracted fields in a dim light; posterior polar cataracts and a pigmented retina. The greyish appearance of the retina is noted, and also the presence here and there of white spots in the retina. No consanguinity. Bibl. No. 43.

Fig. 72. *Ayres' Case.* II. 2, aged 37 years, a widow, had been unable to see well at night since childhood but was able to earn her living by doing plain sewing. On examination it was found that L.V. = R.V. $= \frac{1}{2}\frac{5}{5}$; there was a small posterior polar cataract in each lens; the vessels of the retina were considerably diminished in size, and pigment was sparsely scattered over the retina, the greater portion of it being on the inner side; she was the third child in a sibship of five. III. 1, daughter to II. 2, aged 15 years, had the same defect; R.V. = L.V. $= \frac{1}{2}\frac{5}{0}$; the retinal vessels were slightly diminished and she had less pigment in the retina than her mother. III. 2, aged 12 years, had some difficulty in seeing at night; for her R.V. = L.V. $= \frac{1}{5}\frac{5}{0}$; she was found to have more pigment in her retina than her sister or mother. II. 3, husband to II. 2, had good eyes. No consanguinity. Bibl. No. 138.

Fig. 73. *Tobin's Case.* II. 2 and 3, two healthy and energetic "near relations," married and had twelve children, five girls and seven boys, of whom III. 1, a son, aged 47, is healthy. III. 2, Nancy, aged 42, was born deaf and with bad sight, she is unable now to follow the finger alphabet, and has been unable to read for ten years. III. 3, 4, 5, 7 and 8 are normal. III. 10, Jane, aged 32, with dark hair and brown irides, is an intelligent deaf-mute, and has retinitis pigmentosa with very defective vision and night-blindness: her fields are reduced to a circle of 10° round the fixation point and are even smaller for colours; the retinal vessels are diminished in size and their walls thickened, there is no atrophy of the disc; pigment is abundant at the periphery and scattered masses extend to the neighbourhood of the disc; she has a posterior polar cataract. III. 11 and 12 are two healthy sons. III. 13, a son, aged 25, is a deaf-mute with retinitis pigmentosa, masses of black pigment in a lace-like pattern form a complete circle round the retinal periphery; he is night-blind and can only read in a bright light, his sight has been gradually failing for some time. III. 14, a son, aged 22, is a deaf-mute with retinitis pigmentosa; he is night-blind, his sight began to fail in childhood and now he can scarcely see to read or write; pigment is abundant; the retinal vessels are reduced to threads and his fields are markedly contracted.

The mother came of healthy parents and died, aged 50, of heart disease. The father also came of healthy parents and had ten healthy siblings. Two normal daughters of the sibship married and had healthy families. One other normal daughter was examined and found to have slight astigmatism. Consanguinity. Bibl. No. 131.

Fig. 74. *Webster's Case.* Four cases of retinitis pigmentosa in a sibship of four, the mother and three cousins being also affected. II. 6, aged 44, had always been troubled with night-blindness and for several years had found difficulty with his sight in the day also; R.V. = $\frac{20}{200}$, L.V. = $\frac{20}{30}$; visual fields were nearly circular and very small; retinitis pigmentosa was very marked in both eyes; he had also floating bodies in the vitreous and a R. posterior polar cataract. No consanguinity. Bibl. No. 105.

Fig. 75. *La Gleyze's Case.* (Taken from Nettleship.) Retinitis pigmentosa in two brothers. II. 6 and 7, aged 12 and 10 years respectively (1903). II. 4 and 5 were miscarriages; II. 8 represents six other children of whom details are given. II. 1—3 are three siblings, maternal first cousins to II. 6, 7, who were all affected by congenital cataract, one was operated on and the fundus was then seen to be normal. The parents of each sibship were first cousins. Consanguinity. Bibl. No. 251, p. 344.

Fig. 76. *Webster's Case.* Three cases of retinitis pigmentosa in a sibship of seven. III. 1, 4 and 5 had no eye trouble. III. 6, aged 33, had worn glasses for ten years for reading only. III. 2, aged 49, had always had bad sight and became blind at the age of 25, he had characteristic pigmentary deposits over the whole fundus, atrophy of the optic nerves and posterior polar cataracts in both eyes. III. 3, aged 46, had no cataract, no marked atrophy of the discs, was still able to do her own housework, but had marked retinitis pigmentosa; she married and had three children who died in infancy. III. 7, aged 30, could see to work on a farm up to the age of 15; he had retinitis pigmentosa with atrophy of the discs and posterior polar cataract, bilaterally. The paternal grandfather, I. 2, had "inflammation in his eyes from a cold" and was blind for several years before his death at the age of 76. A paternal great-aunt, I. 3, was blind from her youth. No consanguinity. Bibl. No. 105.

Fig. 77. *Picard's Case.* Two healthy first cousins have three children, of whom II. 1, a robust youth aged 21, who had had trouble with his sight since early infancy, was found to have retinitis pigmentosa with narrowed retinal vessels, atrophy of disc and typical deposits of pigment in the retina; he had contracted fields, diminished visual acuity and night-blindness, also a posterior polar cataract on the left side. II. 2 was delicate and had suffered from night-blindness since infancy. II. 3 was deaf and had severe attacks of neuralgia. Consanguinity. Bibl. No. 64.

Fig. 78. *Mellinger's Case.* II. 1, aged 38, had suffered from his eyes during his school days and had always seen badly at night; R.V. = L.V. = $\frac{2}{7}$; media clear except for a bilateral posterior polar cataract; the papillae were very pale; the vessels very narrow; the characteristic bone corpuscle type of pigment commenced near the papillary margin, the deposits sometimes being thickly massed and sometimes more dispersed; towards the equator the retina was free from pigment; the fields had almost normal boundaries but on each side was found a zone in which the sight was bad. He had a sister who suffered from night-blindness. The parents and grandparents were unrelated but a sibling of one of the grandmothers was said to have suffered from weak eyes. No consanguinity. Bibl. No. 156.

Fig. 79. *Priestly Smith's Case.* Four cases of retinitis pigmentosa in a sibship of seven, associated with deafness and with posterior polar cataract Generations I. and II. were known to be healthy, and to have good sight and hearing. III. 1 was strong, hearing perfect, vision normal. III. 2, died, aged 25, from injury, had good sight and hearing. III. 3, aged 48, nearly deaf and dumb, was irritable and passionate; she was night-blind and her sight failed gradually until she had only perception of light; the fundus in each eye was partly hidden from view by posterior cortical cataracts; she had advanced retinitis pigmentosa. Her mother, II. 1, had a severe nervous shock in the early months of her pregnancy with III. 3. III. 4, died, aged 18 months, of croup. III. 5, aged 41, had advanced retinitis pigmentosa, was nearly deaf and had posterior polar opacities in each lens. III. 6, aged 38, not examined, was reported to be nearly deaf and partly blind. III. 7, aged 33, had advanced retinitis pigmentosa, was very deaf and had posterior polar cataracts; he married and had four children, aged 12 to $2\frac{1}{2}$, all with perfect sight and hearing. No consanguinity. Bibl. No. 115.

Fig. 80. *Liebreich's Case.* I. 2, a healthy soldier, who was however addicted to drink, married twice; by his first wife he had two normal children; by his second wife he had five children of whom three, two females and one male, were deaf-mutes with retinitis pigmentosa, one female and one male were normal I. 2 further, had an illegitimate son by the younger sister of his second wife, born between the second and third legitimate children, who was also a deaf-mute with retinitis pigmentosa. No consanguinity recorded. Bibl. No. 42.

Fig. 81. *Derby's Case.* III. 1, aged 14, had retinitis pigmentosa; pigment was profuse, nerves "muddy," vessels small, V. = 0·3 in each eye, fields greatly contracted; at the age of 19 he was found to be getting rapidly worse and vision was reduced to 0·1 in each eye. His father, II. 2, had bilateral posterior polar cataract, he, and also III. 2, 3 and 4, had divergent strabismus. The paternal grandparents were first cousins. Bibl. No 149.

Fig. 82. *Rosenbaum's Case.* Retinitis pigmentosa and incipient cataract in I. 1, aged 56 years. V. = $\frac{8}{60}$. All his children had the same disease. No consanguinity recorded. Bibl. No 213.

Fig. 83. *Kaupp's Case* I. 1 and 2 were unrelated and had normal sight. Of their ten children, II. 1

was a deaf-mute with retinitis pigmentosa, II. 2 represents four children who died young. II. 3 and 4 were normal sons, II. 5 a normal daughter, and II. 6 and 7, both daughters, were deaf-mutes with normal vision. II. 1 was examined at the age of 28 years, and reported that for ten years he had suffered from night-blindness; V. = $\frac{3}{6}$; fields were greatly contracted, and the fundi showed changes typical of the disease. No consanguinity. Bibl. No. 162.

Fig. 84. *Nettleship's Case.* Retinitis pigmentosa and deafness in a girl, IV. 4, who had two normal brothers and one normal sister. A sister of her paternal grandfather, II. 1, was a deaf-mute. I. 1 and 2 were first cousins. The parents, III. 1 and 2, were normal and unrelated. Consanguinity. Bibl. No. 251, p. 29.

Fig. 85. *Lawford's Case.* (Taken from Nettleship.) A single case of retinitis pigmentosa associated with deaf-mutism in a girl, III. 2, who had one normal brother. The parents were first cousins; the grandmothers were sisters, each of whom had many children and grandchildren, all of whom were known to be free from defects of sight, deaf-mutism and mental degeneracy. Consanguinity. Bibl. No. 251, p. 39.

Fig. 86. *Oakley's Case.* III. 2, a stupid heavy looking girl, aged 16, had retinitis pigmentosa and myopia of 4 D., V. = $\frac{12}{60}$. A younger sister and an elder brother, aged 22, were highly myopic but had no retinitis pigmentosa. The parents were first cousins, and were dead, but the grandmother, I. 1, reported that they were both deaf and had very bad sight. I. 1, with good sight, married her second cousin who had bad sight; one of her daughters was the mother of III. 2, and another daughter, who was seen and had myopia, married a near relative and had five children of whom one was deaf and another had disease of the hip joint. It is unfortunate that there is no ophthalmological report of II. 1 and 2. Consanguinity. Bibl. No. 159.

Fig. 87. *Nettleship's Case.* II. 2, died of phthisis, aged 30; his wife, II. 3, an only child, committed suicide from grief at her husband's death; both had good eyes. Of their three children, III. 1 died, aged 3 years, III. 2 was normal and healthy, III. 3 was partially deaf and had, when seen, aged 71, advanced retinitis pigmentosa and cataract. III. 3 had two children, of whom one, IV. 2, had retinitis pigmentosa. IV. 2 had one child, aged 17, with posterior cortical cataract, but no retinitis pigmentosa. The family history was well known for two generations before generation III. No consanguinity. Bibl. No. 251, p. 17.

Fig. 88. *Maes' Case.* Retinitis pigmentosa associated with deafness in three sisters, the first, second and tenth born in a sibship of ten. Seven siblings were normal; the parents were normal and unrelated. One sister only was examined, she had seen quite well as a child, but since her twentieth year her vision had slowly deteriorated; at the age of 44 years her fields were greatly contracted even in bright daylight, but she was still able to read fairly well; media were normal and the retina was pigmented. No consanguinity. Bibl. No. 43.

Fig. 89. *Gonin's Case.* Retinitis pigmentosa in an only child, a deaf-mute aged 17 years, the condition had been diagnosed by Professor Dufour six years previously; visual acuity was $\frac{1}{3}$ for the R. eye and $\frac{1}{2}$ for the L.; she had slight hypermetropic astigmatism; her visual fields were contracted in a reduced light and even in full daylight she had an incomplete annular scotoma in the R. eye; night-blindness was not very pronounced; yellowish spots are described in the equatorial region as well as the typical pigmentation. Her parents were normal, but her maternal aunt was night-blind. No consanguinity recorded. Bibl. No. 215.

Fig. 90. *Webster's Case* 2. Retinitis pigmentosa and deaf-mutism in a boy, aged 16, the offspring of first cousins. Consanguinity. Bibl. No. 105.

PLATE VII. Fig. 91. *Liebreich's Case.* This pedigree is of special interest as being, according to Nettleship (Bibl. No. 251) the first family history of retinitis pigmentosa to be drawn up in support of consanguinity as a cause. The family was that of a noble, and intermarriage had been frequent within it for several generations. I. 1 and 2 were healthy and unrelated; they had one normal son, II. 2, whose descendants in the third and fourth generations were healthy, and two normal daughters who became first and second wives to their normal cousin II. 4. II. 3 died at the birth of her first still-born child. II. 5 had thirteen children, of whom three died in infancy; one, III. 5, died, aged 16, completely paralysed; three had retinitis pigmentosa, and further one of these was an idiot; one, III. 10, married a first cousin once removed, and had seven children, of whom one was an idiot; and one, III. 11, married a cousin and had one feeble-minded child, IV. 3; four normal members either did not marry or had no children. Consanguinity. Bibl. No. 42.

Fig. 92. *Gonin's Case.* Retinitis pigmentosa with typical ophthalmoscopic appearances in two brothers whose six sisters were normal, and whose parents were normal and unrelated. II. 2, aged 28, had greatly contracted fields, and his vision was reduced to finger counting at 2 metres with the R. eye and at 5 metres with the L.; media were transparent; pigmentation of the retina reached nearly to the disc. II. 4, aged 20, had visual acuity of $\frac{1}{6}$ in 1898, and also on a second examination in 1901, he had slight hypermetropia and contraction of fields; other conditions were typical of the disease. The maternal uncle, I. 2, was mentally defective and suffered from night-blindness. There was no syphilis in the family. No consanguinity. Bibl. No. 218.

Fig. 93. *Dean's Case.* Retinitis pigmentosa in three siblings, the mother was healthy and had normal vision, the father was an idiot. II. 1, aged 11 years, could see large objects during the day, but became blind in a dull light; V. = $\frac{6}{9}$; fundus showed changes typical of retinitis pigmentosa; he was exceedingly dull and had defective teeth, only three wedge-shaped incisors being present in the lower jaw. II. 2, aged 9, a very bright boy with normal teeth, had fundi like his brothers; V. = $\frac{6}{9}$. II. 3, aged 6 years, a very stupid little girl, suffered from night-blindness; V. = $\frac{6}{10}$; her fundus showed retinitis pigmentosa; she had been without any upper incisors for 18 months. No consanguinity recorded. Bibl. No. 211.

Fig. 94. *Herrlinger's Case* 86. II. 2, aged 26, had retinitis pigmentosa; he had divergent strabismus and myopia of −4·5 D. for the R. eye, −8 D. for the left, corrected V. = $\frac{5}{30}$ for each. His brother was dead, but was reported to have had bad sight. The parents were first cousins, and the mother, I. 3, had bad sight, but was apparently not examined. The mother's brother, I. 2, was reported to be nearly blind; his children were almost idiotic, and had weak sight. Consanguinity. Bibl. No. 203.

Fig. 95. *Siegheim's Case* 16. Retinitis pigmentosa associated with deaf-mutism in II. 2, all the five siblings, II. 3, were deaf-mutes. The mother, I. 2, had good sight; the father, I. 3, was mentally defective, the state of his vision was unknown. The mother had normal children by her first husband. No consanguinity recorded. Bibl. No. 146.

Fig. 96. *Wider's Case.* Retinitis pigmentosa associated with mental defect and polydactyly in a brother and sister, the only children of normal parents, II. 1, aged 20, when examined had suffered from the disease since early youth; she was hypermetropic, had defective colour sense, greatly contracted fields, V. = $\frac{5}{24} - \frac{5}{18}$, and her fundus showed typical changes; she had six fingers on each hand, and six toes on each foot, and was mentally defective. II. 2, aged 14, when examined had also suffered from the disease for some years; he was myopic, had defective colour sense, concentric contraction of fields, V. = $\frac{5}{36}$, and his fundus also showed typical changes; he had the same associated defects as his sister, and also stammered. No consanguinity recorded. Bibl. No. 137.

Fig. 97. *Cant's Case.* Four cases of retinitis pigmentosa in a sibship of four; the father was epileptic. The disease increased in severity from the youngest, aged 5, whose fundus was dotted with minute pigmentary deposits at the periphery, to the eldest, aged 15, in which case the pigment was much more profuse and extended nearly to the centre of the retina; the retinal vessels were narrowed in the elder children, and the discs were pale. All were hypermetropic, and the two eldest boys had R. internal strabismus; fields of vision were greatly diminished in all; for the eldest V. = $\frac{5}{50}$ and J. 6, in the younger ones V. = $\frac{5}{18}$ and J. 4. All had difficulty in finding their way about in the evening, and saw very badly by artificial light; colour sense was normal. No consanguinity. Bibl. No. 139.

Fig. 98. *Herrlinger's Case* 18. III. 1, aged 39 years, had noticed that he had a marked diminution of vision for four years; he had retinitis pigmentosa, with contraction of his fields of vision; refraction was myopic (−2 D.), R. V. = $\frac{5}{12} - \frac{5}{9}$, L.V. = $\frac{5}{24}$; colour sense was normal. Two of his four siblings and a sister of his grandmother suffered from night-blindness. His parents had good vision. No consanguinity. Bibl. No. 203.

Fig. 99. *Webster's Case.* Retinitis pigmentosa in II. 2 appeared to follow a severe nervous shock due to the death of a daughter. II. 1 had imperfect vision, especially at night; no other members of the family were affected. No consanguinity. Bibl. No. 105.

Fig. 100. *Nettleship's Case.* IV. 1, aged 13 years, had retinitis pigmentosa; her two sisters were normal, her parents were normal and unrelated. III. 3, a first cousin of the father, III. 2, became blind at the age of 16, almost certainly from the same malady; his maternal grandparents, I. 1 and 2, were first cousins. Consanguinity. Bibl. No. 251, p. 28.

Fig. 101. *Mooren's Case.* Retinitis pigmentosa in a boy who was the offspring of uncle and niece, the parents and grandparents having normal vision. Consanguinity. Bibl. No. 114.

Fig. 102. *Herrlinger's Case* 66. IV. 1, aged 8 years, had very weak sight, but was able to go about alone; refraction was emmetropic; he had retinitis pigmentosa with very marked concentric contraction of his visual fields; he had nystagmus. One sister was born blind. The parents were healthy, and were first cousins once removed. No other case of retinitis pigmentosa was known in the family. Consanguinity. Bibl. No. 203.

Fig. 103. *Herrlinger's Case* 39. Retinitis pigmentosa in a brother and sister whose great-grandparents were first cousins. IV. 1, aged 9 years, had seen badly since early childhood; R.V. = L.V. = $\frac{5}{9}$, refraction was myopic; he had defective colour vision and retinitis pigmentosa with some contraction of fields of vision. His only sister was similarly affected. The parents and other relatives were normal. Consanguinity. Bibl. No. 203.

Fig. 104. *Herrlinger's Case* 36. II. 2, aged 66, had had weak sight since her youth; she had retinitis pigmentosa, and her vision was now reduced to finger counting. Her brother who was dead had suffered from night-blindness. Their parents were normal. II. 2 had six children who all saw well, but one of

them married a cousin, and had two boys who suffered from an atypical retinitis pigmentosa. Consanguinity. Bibl. No. 203.

Fig. 105. *Wilbrand and Saenger's Case.* Retinitis pigmentosa in a brother and sister, the offspring of first cousins. Consanguinity. Bibl. No. 264.

Fig. 106. *Rosenbaum's Case.* Retinitis pigmentosa in II. 1, aged 18, he had been night-blind since childhood; fundi were typical of the disease; R.V. = $\frac{8}{12}$, L.V. = 1. His father was night-blind. No consanguinity recorded. Bibl. No. 213.

Fig. 107. *Oakley's Case.* I. 1 with retinitis pigmentosa married a near relative; they had seven children, of whom the only survivor, a son aged 27, reported that he had had bad sight since childhood, and had been told at the age of 9 years that he had retinitis pigmentosa. Consanguinity. Bibl. No. 159.

Fig. 108. *Gonin's Case.* In a sibship of seven brothers the first, third and fifth born suffered from night-blindness, which developed about the age of 25 years; the seventh born was at the time of the report only aged 24, but had not so far complained of his sight. The parents were normal and unrelated. One case only was examined, he, II. 3, aged 36, had a visual acuity of $\frac{1}{2}$ for the right eye and $\frac{5}{6}$ for the left; his fields were much contracted in a reduced light, and there was found to be a typical, though not very extensive, pigmentation of the retina, the pigment for the most part was to be seen on the nasal side in the equatorial region. No consanguinity. Bibl. No. 215.

Fig. 109. *Rosenbaum's Case* 20. Retinitis pigmentosa in six members of a sibship of eleven. No consanguinity recorded. Bibl. No. 213.

Fig. 110. *Wilbrand and Saenger's Case.* Retinitis pigmentosa in two siblings who had two deaf siblings, the parents were blood relations. Consanguinity. Bibl. No. 264.

Fig. 111. *Wilbrand and Saenger's Case.* Unilateral retinitis pigmentosa in a man aged 46. II. 2, aged 46, had V. = $\frac{6}{9}$ for the left eye which was ophthalmoscopically normal; for the right eye V. = fingers at 2·5 m., he had a posterior cortical cataract and retinitis pigmentosa. At the age of 14 the patient had noticed by chance that he saw badly with his right eye, and he believed that the vision had remained much the same since that time, he was night-blind in that eye, and the field of vision was contracted almost to the fixation point; with Förster's photometer after 10 minutes adaptation he could see through an opening of 2 mm. with the left eye, but with the right eye he required an opening of 22 mm. after 32 minutes adaptation. A sister, aged 51, was almost blind, and was deaf. Syphilis was apparently not present. No consanguinity. Bibl. No. 264.

Fig. 112. *Herrlinger's Case* 92. Retinitis pigmentosa in a girl aged 16 whose parents were second cousins, her two grandmothers were first cousins; her father saw badly by day and by night, but was apparently not examined; her three siblings were healthy. II. 1 had suffered from night-blindness from an early age; she had slight myopia, R.V. = $\frac{5}{9} - \frac{5}{6}$, L.V. = $\frac{5}{7\cdot5}$; colour vision was normal, and there was concentric contraction of her fields of vision. Consanguinity. Bibl. No. 203.

Fig. 113. *Derby's Case.* II. 1 was seen, aged 3, his parents having noticed imperfect vision at night for 15 months; the child was restless and difficult to examine, and the ophthalmoscope revealed nothing. Five years later the child with his sister, II. 2, aged 7, were seen; each was night-blind, and showed changes typical of retinitis pigmentosa; their visual fields were contracted, V. = 0·2 for II. 1 and 0·4 for II. 2. Both patients showed improvement under treatment with constant current. No further cases of retinitis pigmentosa were known in the family. No consanguinity. Bibl. No. 149.

Fig. 114 *Höring's Case.* I. 1 and 2, a healthy and normal brewer and his wife living in comfortable circumstances in a healthy district, had five children. The three eldest, aged 15, 12 and 11 years respectively, were normal, the two youngest, a girl aged 9 and a boy aged 5, were extremely stubborn and difficult in temperament, the girl had six toes on each foot, and six fingers on her left hand, the boy had twelve toes and twelve fingers, and they both suffered from night-blindness, with fundal changes typical of retinitis pigmentosa. No consanguinity recorded. Bibl. No. 49.

Fig. 115. *Wilbrand and Saenger's Case.* II. 2, aged 23, had retinitis pigmentosa, he had seen and heard badly since birth; R.V. = L.V. = $\frac{6}{18}$; the fields of vision were greatly contracted. His eldest sister, aged 34, also had bad sight and hearing; his eight other siblings had normal vision, but two of his younger sisters were epileptic. The father was a great drinker. No consanguinity. Bibl. No. 264.

Fig. 116. *Leber's Case.* Retinitis pigmentosa following an extremely rapid course in three consecutive siblings, a girl and two boys. The disease appeared when they were aged 6 or 7 years, and after from 9 to 18 months each was completely blind; there was no associated night-blindness in these cases. No consanguinity recorded. Bibl. No. 98.

Fig. 117. *Harlan's Case.* Seven cases of retinitis pigmentosa in a sibship of twelve. II. 1, aged 38, could distinguish large letters till the age of 18, but was now absolutely blind; pupils dilated and fixed, external strabismus. II. 2, aged 28, could read large letters till the age of 20, she can now just distinguish day from night; pupils dilated and fixed, strabismus. The ophthalmoscopic appearances were very beauti-

fully marked in both cases. Seven out of the twelve children of this sibship were born partially blind, the condition increasing with age. II. 3—7 are not so blind as the two described above. Parents were healthy and lived to old age. No cases of retinitis pigmentosa were known in previous generations. No consanguinity. Bibl. No. 82.

Fig. 118. *Fergus's Case.* II. 1 had retinitis pigmentosa diagnosed twenty years ago; she had been unable to read or write for twelve years, and her vision was now reduced to a very faint perception of light and shade. The author describes various subjective colour phenomena experienced by the patient, and is of the opinion that they indicate the last stages in the destruction of the retinal function. One brother and two maternal relations were also affected. Four living siblings had normal vision, five siblings were dead. The parents were first cousins. Consanguinity. Bibl. No. 288.

Plate VIII. Fig. 119. *Usher and Smith's Case.* This pedigree is of very special interest, for it is the only example found in the literature of the subject showing the result of intermarriage between two individuals, one of whom was suffering from retinitis pigmentosa and the other from congenital stationary night-blindness without fundus changes; of the four children born of these parents two had normal fundi, one had choroideremia, and one had typical retinitis pigmentosa. We are greatly indebted to Usher for allowing us to publish the beautiful colour sketch which he had prepared showing the appearance of the fundus in the case of choroideremia: we believe it to be the first coloured plate of the condition to be published in this country. See Plate B.

IV. 7, Alexander E., aged 24 (1914), was a butchers' messenger boy; he had no history of serious illness, but had been delicate as a child, was irritable, slept badly at night, and required much attention; he was subject to chilblains on ears and fingers; he had been night-blind as long as he could remember, but reported that his vision was no worse than it had always been. There was nothing abnormal about the eyes externally, though when dilated the pupils were of a pale reddish apple jelly colour; refraction: R. myopia 4 D. in horizontal meridian, 6·5 D. in vertical meridian, V. with correction = $\frac{6}{18}$; L. myopia 3·5 D. in horizontal, 5 D. in vertical meridian, V. with correction = $\frac{6}{24}$. Night-blindness was marked; fields of vision, tested with a 10 mm. white square in good daylight, were contracted to within 10°, though in the left field there was a narrow seeing area down-out extending to 50°; result of tests for colour vision were unsatisfactory and not uniform. Ophthalmoscopic examination showed small opacities in both lenses and a single small translucent floating opacity in each vitreous. The appearances in each fundus were similar; the light reflected into the pupils at one or two feet distance produced a white reflex which became pink when he fixed the mirror; on direct or indirect examination most of the fundus of each eye appeared to be white; at some parts, especially near the discs, there was very faint mottling, just an indication that the white was not quite uniform. The optic disc had a good red colour; there was no physiological cup, and the edge of the disc was not clearly defined. The retinal vessels were little, if at all, narrowed, no white lines were seen along their edges, they had a normal distribution. The vorticose veins were conspicuous, most of them received branches from peripheral parts of the fundus only, but vessels from the macular region communicated with branches of some of them; some of the vorticose veins disappeared suddenly, others appeared to gradually pass more deeply into semi-translucent white tissue. Close to the outer edge of the left optic disc was a large congeries of very small tortuous blood-vessels closely packed together, which converged towards a few large vessels at the edge of the plexus believed to be veins draining the macular plexus formed presumably by posterior ciliary arteries; some retinal vessels passed in front of the vessels in the plexus, but none were found to anastomose with them. At the macula of the right eye was a much smaller congeries of similar vessels partly covered and largely hidden by a fairly homogeneous red layer with scanty pigment; no vessel passed from the edge of the optic disc to either plexus; no vessels were seen which correspond to the long ciliary arteries. Some pieces of branched pigment were scattered sparsely over the fundus. At the extreme periphery of each fundus were a few narrow areas of dark red fundus visible with widely dilated pupils, they were in marked contrast with the rest of the fundus, their margins, usually well defined, were irregular and formed bays, and at some parts choroidal vessels passed from beneath them to the venae vorticosae. There were a few small islands of what seemed to be pigmented retinal epithelium to judge by their colour and relation to retinal vessels. A detailed account of the physical condition of the patient and of former examinations of his eyes are given by the author. Of the siblings of IV. 7, a sister, aged 26, IV. 5, and a brother, aged 24, IV. 6, had normal fundi and good vision. A younger sister, IV. 8, aged 22 (1912), suffered from night-blindness; refraction: R. myopia 1 D. in vertical and hypermetropia 2 D. in horizontal meridian, V. with correction = $\frac{6}{18}$; L. myopia 5 D. in vertical and hypermetropia, 2 D. in horizontal meridian, V. with correction = $\frac{6}{12}$; media were clear; optic discs possibly rather too pale, arteries narrowed; the periphery of each fundus was studded with dark moss-like pigment; no patches of choroidal atrophy were present; fields showed incomplete relative ring scotoma, and were contracted; Wassermann test negative. She and her brother, IV. 7, were fat, heavy and expressionless, their two normal siblings were more fresh and alert.

The father of this sibship, III. 7, aged 54, had congenital night-blindness without fundus changes, and was myopic. For him fields of vision were full, colour sense normal, media clear, discs and retinal

vessels were normal, and there was no retinal pigmentation; he had myopia in each eye of 7·5 D., R.V. with correction = $\frac{6}{18}$, L.V. with correction = $\frac{6}{12}$ partly; night-blindness was marked. He was twice married, but had no children by his second wife.

The mother, III. 41, died in 1910 of heart disease; she was the illegitimate child of II. 17 and probably II. 18; her fundi had been examined and retinitis pigmentosa diagnosed in 1905; her husband reported that she saw well at night. No cases of night-blindness were known in the ancestors of III. 41, but her mother, II. 17, appears to have been dissolute, and seldom sober after the death of her husband. A maternal uncle of the father, II. 1, was reported to have been night-blind from his earliest days, and to have been myopic; information concerning him was obtained from his son, III. 5, who was a medical man, and who did not know of any other case of the defect amongst his ancestry.

A considerable number of the normal members of the pedigree were examined by the author, and information concerning them is given in the original history. No consanguinity. Bibl. No. 310.

Fig. 120. *Nettleship's Case.* Retinitis pigmentosa in at least four children in a sibship of eight, the offspring of first cousins. IV. 1 and 2 were affected girls, IV. 3 and 5 were affected boys; IV. 6 and 7 were too young to test, IV. 8 died aged 10 months. The parents were normal, their fathers, II. 2 and 3, were brothers; their mothers, II. 1 and 4, were remotely connected also. Consanguinity. Bibl. No. 251, p. 37.

Fig. 121. *La Gleyze's Case.* (Taken from Nettleship.) Two cases of retinitis pigmentosa in the offspring of uncle and niece. Parents and grandparents were normal, but two of the father's first cousins, II. 4 and 5, had retinitis pigmentosa. Consanguinity. Bibl. No. 251, p. 28.

Fig. 122. *Siegheim's Case.* Retinitis pigmentosa in IV. 1, sex not given. One brother had weak sight and was night-blind, two brothers and one sister were normal. The father had normal vision, the mother had "weak" sight, one maternal uncle was blind, two aunts and one uncle, siblings of the mother, had normal vision. The maternal grandfather and great-grandfather were blind. It is to be regretted that only one case was apparently examined, and so little information is given of the other affected members of the family. No consanguinity recorded. Bibl. No. 146.

Fig. 123. *Nettleship's Case.* Seven cases of retinitis pigmentosa in a sibship of eight, III. 1—8. Of the affected members four were males, three were females; the unaffected member of the sibship was a male. The parents were normal and unrelated, but a maternal great-uncle had retinitis pigmentosa. No consanguinity. Bibl. No. 251, p. 18.

No. 124. *Leber's Case.* Retinitis pigmentosa in a boy whose grandfathers were brothers, and whose grandmothers were sisters; his three siblings were normal. The boy, aged 12 years, was blind; fine spots of pigment were scattered over the whole fundus, and occasionally pigment flecks of the bone corpuscle type were to be seen along the retinal vessels; the vessels, especially the arteries, were greatly narrowed; the boy also had some defect in his speech. Consanguinity. Bibl. No. 72.

Fig. 125. *Smyth's Case.* (Taken from Nettleship.) Two cases of retinitis pigmentosa in a sibship of six. III. 1, 3 and 4 were living, and had perfect sight; III. 2, twin to III. 1, died soon after birth. III. 5, a boy aged 10 years, had been noticed to be night-blind at the age of 2, he now had typical retinitis pigmentosa. III. 6, a boy aged 4, was night-blind at the age of 3 years, and now had a few patches of pigment at the periphery of each fundus, with somewhat shrunken retinal arteries. The parents were normal and unrelated. There was a history of phthisis in the mother's maternal aunt, I. 4, in her paternal uncle, I. 1, and in three of her paternal cousins, II. 1, 2, 3. No consanguinity. Bibl. No. 251, p. 354.

Fig. 126. *Rosenbaum's Case.* Retinitis pigmentosa in two brothers whose paternal grandparents were first cousins. III. 1 was seen, aged 9, when he was suffering from phlyctenular conjunctivitis, the fundi were then normal; three years later he was night-blind, and had typical retinitis pigmentosa with visual acuity reduced to $\frac{6}{36}$; the disease progressed rapidly in his case. III. 2, aged 8, was seen with typical retinitis pigmentosa; for him V. = $\frac{1}{2}$. Consanguinity. Bibl. No. 213.

Fig. 127. *Rosenbaum's Case.* Retinitis pigmentosa in III. 1, aged 20 years; V. = $\frac{6}{24}$; fields greatly contracted; the pigmentation of the retina reached almost to the macula region. The father, grandfather and a paternal uncle suffered from night-blindness. No consanguinity recorded. Bibl. No. 213.

Fig. 128. *Oakley's Case.* Retinitis pigmentosa in three, probably in four generations. III. 3 seen, aged 46, was anaemic, but had always had fairly good health, he was wearing spectacles of − 5 D. for myopia, and had been told twenty years previously that he had retinitis pigmentosa; the disease made very little progress until a year ago, when his sight became rapidly worse. His parents, II. 2 and 3, were first cousins, and his father, who died aged 56, had bad sight, and was nearly blind at the time of his death. He believed that his grandfather's sight was also very bad. His mother and her three daughters by a second marriage were all examined and found normal. The younger brother of III. 3 by the first marriage also had retinitis pigmentosa. The paternal aunt, II. 4, had retinitis pigmentosa, married her first cousin, and transmitted the disease to one of her six children. III. 3 married his first cousin with normal eyes, and had two children, a son aged 14 years with retinitis pigmentosa and myopia, and a daughter with normal eyes. Consanguinity. Bibl. No. 159.

Fig. 129. *Leber's Case.* Retinitis pigmentosa in four generations. IV. 2, aged 26 years, had seen badly and been under treatment since boyhood; he suffered from night-blindness, which had apparently not progressed recently; the discs were whitish in colour, and oval in shape, and were surrounded by a ring of choroidal atrophy; the vessels were narrowed, and there were pigment flecks lying along the retinal vessels; choroidal vessels showed very distinctly. The elder brother of IV. 2 was said to be similarly affected, also his mother with her brother and sister; his grandmother and his great-grandmother were said to have suffered from the disease, his younger sister had normal vision. No consanguinity recorded. Bibl. No. 72.

Fig. 130. *Ayres' Case.* IV. 1, seen, aged 44 years, had marked retinitis pigmentosa, the pigment extending to the disc, and the field of vision being reduced to the point of fixation; his only sister had normal eyes. III. 5, mother of IV. 1, died, aged 66 years, and was blind for several years before her death from the same disease; two of her sisters had normal eyes, one sister and one brother were nearly blind. II. 2, maternal grandmother to IV. 1, aged 89 years, had been blind for many years. I. 2, maternal great-grandmother to IV. 1, and one or two of her brothers were blind. It is unfortunate that only one case apparently, in this interesting pedigree, was examined. No consanguinity. Bibl. No. 138.

Fig. 131. *Ayres' Case.* II. 1, a negro, aged 45, had been night-blind for more than twenty years; he had myopia of 2·5 D. for R. eye, 3 D. for L. eye; fields of vision were contracted, and the fundus showed typical retinitis pigmentosa at a rather advanced stage. He had several normal siblings. This was the only case of retinitis pigmentosa seen by the author in a coloured race. No consanguinity. Bibl. No. 169.

Fig. 132. *E. Schmidt's Case.* II. 4, aged 9, and II. 5, aged 5, were said to have retinitis pigmentosa and nystagmus, and to have one sibling who also had bad eyes. Two children of some distant relation of the father were blind, and also the brother of this relation had a blind child. The mother's brother had two blind children. It is unfortunate that no further information was given concerning the nature of the blindness in these cases. No consanguinity in parents or grandparents of II. 4—6. No consanguinity recorded. Bibl. No. 163.

The Usher Series of Pedigrees of Retinitis Pigmentosa.

The following forty-one pedigrees, all worked out by Usher, are of the greatest value both as a collection and also for the wealth of detail which has been given for the individual cases and histories. An extensive family history was taken for forty-one consecutive cases of retinitis pigmentosa seen by the author, (who only omitted a few cases for which no information could be obtained or in which the diagnosis was doubtful), in order to demonstrate whether or no the marked tendency to inheritance of this disease indicated by published histories was to some extent due to selection of cases, authors generally tending only to publish pedigrees in which several members were known to be affected. Nettleship had noted many apparently isolated cases, but he suspected that if sufficient were known of the antecedents of such cases, a hereditary origin could often be demonstrated for them. Usher has clearly shown that such isolated cases do undoubtedly exist, and that in them the defect is not an inherited one; such cases, however, in no sense weaken the significance of the marked hereditary nature of the disease in certain stocks.

We have reproduced many of the pedigrees of this series in full, some of those for isolated cases have only been included in our collection in an abridged form, not indeed from any lack of interest and appreciation for such pedigrees but partly on account of space and cost of reproduction, and also because we hope this will encourage the student of heredity to study the author's original work which contains a great wealth of information the significance of which can be grasped from the author's description far better than from any reproduction.

Usher examined and described a great number of normal as well as affected members in all the families concerned; Wassermann tests were made on many individuals and the most careful enquiry was made throughout for associated defects in affected or unaffected branches of the stocks.

PLATE IX. Fig. 133. *Usher's Case* 14. One case of retinitis pigmentosa and two cases of coloboma of the optic nerve in a sibship of thirteen, also a case of retinitis pigmentosa in a sibship of seven in the same generation. IV. 49, aged 25 (1910), was less robust than his siblings though he had no history of serious illness or bleedings and was not subject to cold fingers and toes; he was night-blind, and defect was first noticed in his vision after he went to school; media clear, discs pale, retinal arteries very narrow and moss-like pigmentation of retina most abundant towards the periphery was in relation to veins and not arteries; no spots or patches of choroidal atrophy; close to inner edge of R. disc were three small grey slightly raised bodies: refraction was hypermetropic, with correction R.V. = $\frac{6}{12}$, L.V. = $\frac{6}{18}$; fields of vision were not contracted but a complete absolute ring scotoma was present in each; Wassermann test negative. His sister, IV. 45, aged 30 (1910), had been married for six years but had no child, she was examined by

Dr Souter; the L. eyeball was smaller than R.; there was defective outward movement of each eye and lateral nystagmus on lateral movement of eyes; in the central part of each fundus there was a circular white area several times the size of a normal disc, it had a well-defined margin, retinal vessels converged to a part near its upper edge; two small white patches of choroidal atrophy were present below this area in R. eye and some choroidal atrophy was present at same position in L.; coloboma of optic nerve was diagnosed; the rest of the fundus, the lenses and irides were normal; the refraction was hypermetropic, corrected vision for R. $= \frac{6}{36}$, for L. $= \frac{6}{60}$. R. field of vision had a large defect above extending from the periphery nearly to fixation point. IV. 46, male, aged 31 (1912), had constant lateral nystagmus; the R. eye was microphthalmic and its disc was replaced by a large crater-like depression two or three times the size of the normal disc, with some choroidal atrophy adjoining its lower part; there were opacities at outer and posterior parts of lens; refraction was hypermetropic; V. with correction = finger counting; the left O. D. was larger than normal, refraction myopic, 6 D.; corrected vision $= \frac{6}{36}$; large sector absent at upper part of field of vision; no night-blindness. Of the other siblings seven of whom were examined all had normal fundi and good vision. IV. 43 was myopic, R. 1·5 D. in oblique meridian, 2·25 D. in opposite meridian, L. 2 D., corrected V. $= \frac{6}{6}$ in each. The children of all the siblings had normal fundi except V. 30, a boy, aged 12 (1908), who had hydrocephalus and double optic atrophy. The mother, III. 43, her parents, II. 22 and 29, and one of her grandparents, I. 3, had good sight, little was known of I. 4. The father, III. 24, his parents, II. 9 and 17, and his grandparents, I. 1 and 2, saw well, but a grandchild of II. 9 by another wife, II. 4, had retinitis pigmentosa. Thus IV. 24, female, aged 32 when seen, had always been night-blind, she had no history of illness or bleeding; retinal vessels showed some narrowing, O. D.'s no marked pallor, choroidal vessels exposed only at periphery; in each eye a small area below showed retinal moss-like pigmentation; some vitreous opacity; the fields were contracted at upper part, at some parts below they were full, but there was a commencing ring scotoma below in each; refraction hypermetropic, corrected V. $= \frac{6}{12}$ in each; Wassermann test positive, she lived in a remote country place and had no appearance of syphilis. Siblings of IV. 24 all saw well. II. 4 suckled III. 24 at the same time that she was suckling her own son, III. 11, and the night-blindness in the offspring of these two was attributed to the mental shock of II. 4 when she learned that III. 24 was her husband's illegitimate child. III. 11 had a normal fundus and good vision, Wassermann test negative, his wife also had good sight.

The only further defects known in this extensive pedigree are deaf-mutism in IV. 66, a second cousin of IV. 49, he was a shoemaker and was not night-blind; myopia in IV. 10, first cousin to IV. 24, and in V. 43. No consanguinity. Bibl. No. 301.

Fig. 134. *Usher's Case* 19. A very extensive pedigree showing two cases of retinitis pigmentosa in a sibship of six, a third case in another sibship of the same generation, and a fourth case in a sibship of the previous generation. V. 13, a fisherman, aged 31 (1908), had noticed that he had defective vision especially at night for three years; he had marked retinal pigmentation especially at inner part of fundus, narrowed retinal arteries and contracted fields; with correction of + 1D. for R. and + 2D. cyl. for L., R.V. = L.V. $= \frac{6}{24}$; seen again in 1912 when he had just returned from a lunatic asylum the condition had progressed; he had had no illnesses or severe bleedings; Wassermann test negative; he was married and had three young children who had normal vision. V. 15, aged about 33 (1912), was very weak mentally and physically, and marked night-blindness had been noticed when he went to school; he read print about the size of 1 J.; fields of vision were much contracted; retinal vessels narrowed; discs pale; extensive typical retinal pigmentation; Wassermann test negative. Of the siblings of V. 13 and 15 one died, V. 20, three had good vision, and V. 19, who was examined had a normal fundus; the children of V. 17 saw well. The parents, IV. 4 and IV. 22, were normal, and the father, IV. 22, had three unaffected children by his second wife. The mother's parents, her grandparents and one great-grandparent had good vision; II. 2, her grandfather, was noted for his bad temper; there were three cases of mental defect in this branch of the family, V. 1, and two cases of myopia, V. 1 and 3. The father's parents, his grandparents, and one of his great-grandparents, I. 12, had good vision, his father, III. 22, became mentally affected at the age of 45, but recovered; the father of III. 23 is doubtful. Of the father's eight siblings seven were normal, one had congenital ptosis, III. 32; one of his great-nephews, VI. 13, had spina bifida.

V. 42, female, aged 16 (1912), had always had difficulty in seeing in a dim light, appearances of both fundi were quite typical of retinitis pigmentosa (case described by the author); Wassermann test positive. Of her siblings V. 39 died aged 3 months; V. 40 was mentally defective and showed evidence of hereditary syphilis, retinal vessels were narrow, discs pale, moss-like pigmentation was present at the periphery in R., in L., a myopic eye, there was dense black pigment, not moss-like, at lower and outer part of fundus only; R.V. = finger counting, L.V. = 1J.; no night-blindness. V. 41 had choroido-retinitis at the age of 3 (1894), when seen in 1913 there was choroido-retinitis affecting the whole fundus, the macula being least affected; R.V. $= \frac{6}{18}$, L.V. = no perception of light. V. 43 had a normal fundus. The mother of this sibship, IV. 58, had no miscarriages but had been treated for syphilis, she had a normal fundus and good vision. The father, IV. 46, was reported to have had venereal disease, he was alcoholic; one of his brothers, IV. 45, was in a lunatic asylum, his other siblings and the children of two of them had normal vision. The maternal grandparents of V. 42 were first cousins, they and their parents had normal vision; the ancestry on the

father's side in the direct line was normal, but several cases of mental defect occurred in the collateral branches.

IV. 14, fisherman, aged 30 (1897), complained of "gradual weakness in both eyes" for 20 years; he had typical retinitis pigmentosa (case described by author); refraction my. R. 7 D. in oblique, 9 D. in opposite meridian, corrected V. $=\frac{6}{18}$, for L. 5 D. in horizontal, 6 D. in vertical meridian corrected V. $=\frac{6}{18}$; he was seen again in 1904 and 1906, in 1912 he was dead; Wassermann test not taken. Three of his siblings, IV. 9, died young from croup, IV. 13 was peculiar, seldom did any work and wandered about with a gun aimlessly. The parents of this sibship were first cousins, they, their parents and grandparents were reported to have normal vision.

For further cases of mental defect in the more distant relatives of the affected sibships, see the pedigree or the author's original account of the family. I. 6 was related to the sibship I. 12—19, they were probably first cousins; there were no fewer than 19 cousin marriages which were not indicated in the pedigree as the figure became too complicated. Consanguinity. Bibl. No. 301.

Fig. 135. *Usher's Case* 3. Possibly three cases of retinitis pigmentosa and one case of congenital ptosis in a sibship of twelve. IV. 36, female, aged 30 (1897), had always had bad sight, her vision had got gradually worse, she was night-blind, and retinitis pigmentosa was diagnosed at this date. In 1912 R.V. $=\frac{1}{60}$, L.V. $=\frac{2}{60}$, no myopia; fields of vision very much contracted; posterior cortical lens opacities were present and the appearance of each fundus was typical of retinitis pigmentosa; Wassermann test negative; she was a gloomy individual with no history of illness or bleedings. Of her siblings, IV. 26, a male, had a stillborn child; IV. 28 had some nose trouble, she and her six children saw well; IV. 29, a male, who died aged 30, was reported to have had defective sight similar to that of his sister; IV. 30 died, aged 37, of appendicitis, she and her six living children had good vision; IV. 32 was not strong, she was married but had no child, her sight was good; IV. 33 was healthy but had some nasal trouble, she had an illegitimate daughter who had a child; IV. 35 had weak sight though not so pronounced as in IV. 29 and IV. 36, he was of strong build and died, aged 24, in a lunatic asylum, nothing had been noticed to be the matter with him until one warm day in August when working in the hayfield he suddenly complained of pain in his head, and all at once became insane, he died a few days afterwards; IV. 38 was not very strong, but he and his ten children saw well; IV. 40 died in infancy; IV. 41 had had ozaena and depressed bridge of nose as long as she could remember, her nine children were healthy and saw well; IV. 44 had congenital (partial) ptosis on the right side, he and his three children saw well.

Of the ten children of IV. 36 five had normal vision, V. 41, 44, 46, 47, 48; V. 49 was a miscarriage; V. 50 had a normal R. fundus, the left optic disc was twice as large as the right, its outer part pale and cupped (coloboma of optic disc); V. 42, aged 22 (1913), had fields nearly full with a complete ring scotoma in each, in R. field the scotoma is absolute up in and down out and relative up out and down in, in L. field the scotoma is absolute except at inner part at 90°; refraction, as in 1906, my. R. 10 D. in horizontal meridian, 13 D. in vertical, L. 13 D. in horizontal, 16 D. in vertical meridian; corrected V. for each $=\frac{6}{12}$; night-blindness appeared to be present, but was not marked; slow adaptation to dark after coming out of light; the discs were a good colour; retinal arteries of full size; a posterior staphyloma with complete choroidal atrophy was present in each; one spot of pigment at outer part of R. retina was present; had cold hands; Wassermann test positive. V. 43 had myopia R. 3 D., L. 4·5 D.; V. 45 had myopia of not more than 1·5 D. in each.

The parents of IV. 36 were first cousins, they and their parents were healthy and lived to old age with good vision; the father had a deaf-mute first cousin, III. 1, and a first cousin who died of phthisis in middle age, III. 2; the mother had six siblings of whom four died of phthisis, one of these being also mentally defective. I. 1 and 2 lived to old age, but nothing was known of their vision. Further information concerning more distant relatives may be obtained from the original history. Consanguinity. Bibl. No. 301.

PLATE X. Fig. 136. *Usher's Case* 30. Two, possibly four cases of retinitis pigmentosa in a sibship of eleven, three other supposed cases in other generations. III. 6, female, aged 66 (1898), had no difficulty in seeing until the age of 25; she had extensive retinal pigmentation at the periphery, though the extreme periphery was free; retinal vessels were much narrowed, the discs a yellowish white colour, and she had posterior lens opacities; refraction myopic, 9 D. in R., 4 D. in L., with correction R.V. $=\frac{6}{18}$, L.V. $=\frac{6}{36}$; fields of vision concentrically contracted to 10°. III. 13, female, in her dotage (1910), fundi were seen with difficulty, she had small pupils and probable lens changes, but retinal pigmentation could be seen at the periphery; vision had failed gradually, and she was nearly if not quite blind; she had a history of night-blindness. III. 19, was night-blind, he died aged 58, was "always short-sighted; got glasses, but did not benefit by them." III. 3, male, was said to have been affected in the same way as III. 6 and 13. III. 4, female, was bedridden, she had senile cataract, and neither fundus was visible. III. 8 was drowned, aged 32. III. 9, aged 74, was myopic, fundus normal except for crescent in L. III. 12, died in infancy. III. 15 had good sight. III. 17, aged 63, had normal fundi. Parents and grandparents of this sibship had good vision.

IV. 28, the eldest son of III. 13 was "silly," and died in a lunatic asylum; his vision was said to be

"just the same as his mother's." The other three children of III. 13, with their children and grandchildren, had normal vision. IV. 4, the second child of III. 3, aged 62, was myopic, had lens opacities, and was deaf, he had a posterior staphyloma; he was not night-blind, and had no retinal pigmentation; one of his five children, V. 6, was myopic, but had no retinitis pigmentosa or night-blindness. IV. 27, youngest of the ten sons of III. 9, was myopic, but had normal fundi and no night-blindness.

In generation II two members, II. 7, maternal uncle to the affected sibship of generation III, and II. 13, first cousin to II. 7, were both reported to have been night-blind. For further information concerning normal members see the original pedigree and author's account. No consanguinity. Bibl. No. 301.

Fig. 137. *Usher's Case* 34. Probably two cases of retinitis pigmentosa in a sibship of four, the offspring of first cousins, in a pedigree where there has been much intermarriage. V. 15, a sullen and morose fisherman, aged 31 (1899), never had good sight, and it had gradually become worse; he did not see well in a bright light, and his sight was best at sunset and sunrise, sight was bad for some considerable time when he went from a light to a dark place and vice versâ; no serious illness; the retinal arteries were very narrow; there was scanty retinal pigmentation at the periphery of the fundus; the discs were of a uniform red colour; choroidal vessels readily seen; he had low hypermetropia and V. $= \frac{6}{36}$ for each; fields of vision were contracted. In 1909 vision was reduced to finger counting at 7 feet, he had marked posterior cortical cataracts in each, and there was retinal pigmentation over the whole periphery of the fundus; the discs were a good colour, retinal arteries extremely narrow. V. 16 died aged 30, of "consumption"; her vision was defective like her brother's; she was night-blind, and fears were entertained that she would fall over the pier. The two sisters, V. 13 and 14, had normal fundi; V. 13 had four normal children, V. 14 married her first cousin, and had no offspring. The parents, grandparents, and great-grandparents had no known defect of vision, one great-grandparent, II. 9, was mentally affected for eight years before his death. II. 13 had the same name as II. 7—10, but was not known to be related. III. 34, a maternal great-uncle, was latterly mentally affected. No defects of vision were known in generations II. and III. In generation IV. one paternal uncle, IV. 11, and one more distant relation, IV. 15, had myopia; IV. 11 had for years taken large quantities of laudanum, he had eleven children, V. 11, of whom two were myopic, and one was mentally defective. One maternal first cousin, V. 30, was a mentally defective deaf-mute; his parents were first cousins, and he had six normal siblings. One further case of deaf-mutism occurs in the pedigree, V. 36. The husband of V. 14, namely V. 34, her first cousin, had uniocular simple optic atrophy, the rest of the fundus being normal, he had no central scotoma, and tension was normal, but his vision had never been good.

IV. 34 was a cripple; VI. 17, an imbecile, died aged 9; VI. 16, died aged 2; VI. 19, aged 31, had a slight stammer and typical symmetrical lamellar cataract; he had four children with normal vision. Additional cousin marriages, not shown in the pedigree, took place between IV. 39 and 42, V. 32 and VI. 25, V. 3 and V. 17. Consanguinity. Bibl. No. 301.

PLATE XI. Fig. 138. *Usher's Case* 9. Two cases of retinitis pigmentosa in a sibship of four, and one case in their half-uncle. IV. 47, male, aged 32 (1909), an exceptionally strong man, was very deaf, and had defective vision which was noticed by his father before he was aged 6; he had marked night-blindness; fields of vision were contracted to 10°; the R. eye could read 1 J. at 11 inches with correction for mixed astigmatism, the L. eye read the same with correction for low myopia; discs were pale, retinal arteries contracted and moss-like retinal pigmentation was all around the periphery; choroidal vessels were much exposed; Wassermann test negative. IV. 49, aged 23 (1905), was very able, and had been first of his year at college; defect in his vision was noticed before the age of 6; he was also very deaf; he was night-blind, and fields of vision were contracted to 10°; refraction R. emm. in horizontal, my. of 1·25 D. in vertical meridian, corrected V. $= \frac{6}{12}$; L. hm. 1 D. in horizontal, my. of 1·75 D. in vertical meridian, corrected V. $= \frac{6}{18}$; opacity at posterior part of lenses; some vitreous opacity; much typical retinal pigmentation; choroidal vessels exposed; pupils reacted sluggishly to light; nystagmus was present; Wassermann test negative. IV. 48 had a normal fundus. IV. 50, aged 19 (1905), had no night-blindness, V. $= \frac{6}{6}$ in each, and fields were full, but there was some narrowing of the retinal arteries, the choroidal vessels were conspicuous at the periphery, and there were some fine granules of pigment in places in the R. periphery of the retina; he had excellent hearing. The mother, III. 55, died, aged 46, of an abdominal tumour, she was not night-blind. The father, III. 29, had a normal fundus, and there was no recorded case of defect in sight or hearing in any of his ancestry. The father of III. 55 had married three times; by his first wife he had three children, of whom one, a male, III. 48, was abroad, but was well known to his cousin, III. 29, he was night-blind, and was reported to be deaf, to lisp; and to have a defective sense of smell. The siblings of III. 48 had good vision. III. 55 was the only child of the second marriage of her father. By his third marriage, II. 39, had three children with normal vision. No other defects were known in this extensive pedigree. Consanguinity. Bibl. No. 301.

Fig. 139. *Usher's Case* 21. Three males and one female, with deaf-mutism and retinitis pigmentosa in the offspring of first cousins, and four further cases, in their cousins, of deaf-mutism and probably retinitis pigmentosa in a sibship, also the offspring of first cousins. IV. 35, male, aged 33 (1906), a deaf-mute, was

in a blind asylum; the discs were pale, the retinal vessels extremely narrow, the choroidal vessels much exposed; extensive retinal pigmentation extended to the O. D.; the fields of vision were very much contracted, and he was night-blind; he had slight hypermetropia; V. for R. = finger counting at 6 feet, for L. = reading 16 J.; Wassermann test negative; his wife was normal, but they had no children. IV. 36, a farmer, was a deaf-mute; he had posterior cortical cataracts; marked retinal pigmentation, discs pale, retinal vessels very narrow, and was night-blind; he could read the newspaper with a high magnifying glass; he had a R. divergent strabismus. IV. 37, twin brother to IV. 36, died, aged 4 months, of teething fever; it was not known whether he was deaf. IV. 38, a deaf-mute, had commencing posterior cortical cataracts, very extensive retinal pigmentation, discs were pale, retinal vessels narrow, and he was night-blind; he had low hypermetropia, and was able to see enough to get about by himself. IV. 39 was stillborn. IV. 40, aged 30 (1911), a very intelligent female, was a deaf-mute; she was night-blind, and had retinal pigmentation confined to the periphery of the fundus; she had some hypermetropia, and enough vision to read the newspaper through a strong glass. None of these cases had a history of severe illness or bleeding; in all the night-blindness was first noticed on going to school; no evidence of syphilis. Of the other siblings, all were believed to have normal sight and hearing, and the fundus was normal in two cases examined, and in two children of the next generation who were examined. IV. 28, died, aged 16, of typhoid fever. IV. 32 was stillborn. The parents, who were first cousins, had good sight and hearing; they died in middle age. The maternal grandmother, II. 11, married three times; by II. 10 she had one child, a son, who died of phthisis, aged 19; by II. 12 she had a daughter, III. 10, the mother of the sibship IV. 25—40; by II. 13 she had three children, III. 20, who died of phthisis, aged 33, III. 22, who was weakly in mind and body, did odd jobs, and was "nearly silly," and III. 23, who died, aged 50, leaving four normal children. The paternal grandmother, II. 18, with good sight and hearing, also married twice; by her first husband, II. 4, who saw and heard well, she had nine children, with no known defects of sight or hearing, though III. 27, who married his first cousin, was father of the sibship IV. 25—40 and III. 30, who married her first cousin, was mother of the other defective sibship IV. 14—23; by her second husband, II. 18, had two sons, of whom one was normal and had two normal children, the other, III. 44, was "silly." I. 1—4 were not known to have any defect of sight or hearing.

IV. 14 was reported to be "soft"; IV. 15—18 were all deaf-mutes and had defective vision, they were abroad; IV. 15, a farmer; IV. 16, died aged 15; IV. 17, died aged 5; IV. 18 was an inmate of an asylum abroad, the medical superintendent reported that she was a deaf-mute, and the sight almost gone, "she no doubt has retinitis pigmentosa." IV. 19—24 and their children had good sight and hearing. The father of this sibship married his first cousin, they both had good sight and hearing, as also had the paternal grandparents II. 5 and 6. Consanguinity. Bibl. No. 301.

Fig. 140. *Usher's Case* 5. Two cases of retinitis pigmentosa in a sibship of seven. III. 1, female, aged 18 (1911), had typical retinitis pigmentosa in each eye; Wassermann test negative; hearing excellent; never had any serious illness; night-blindness was noticed as soon as she could move about; refraction, slight hm., with correction R. V. = $\frac{6}{18}$, L. V. = $\frac{6}{18}$; small posterior cataracts were present; discs were pale and waxy, retinal arteries very narrow, choroidal vessels much exposed; much moss-like retinal pigmentation extended from periphery towards macula and disc; fields of vision much contracted. Her affected sister, III. 3, aged 14 (1911), was first noticed to have defective vision after an attack of bronchitis and inflammation of the lungs at the age of 3; she had marked night-blindness; retinal arteries very narrow; choroidal vessels much exposed; in 1906 retinal pigmentation was present in the left periphery only, in 1911 there was a considerable amount present in the right eye also, though less than in the left eye at the same date; fields of vision were much contracted, the left more than the right; refraction my. 1·5 D. in oblique meridian 4 D. in opposite meridian for each eye, corrected V. for each eye = $\frac{6}{36}$. Of the siblings of III. 1 and 3 two brothers were examined and seen to have normal fundi, two brothers died in infancy, and one brother, III. 7, was seen, aged 1 day, when fundus examination was unsatisfactory.

The parents, grandparents, great-grandparents, and five great-great-grandparents were believed to have normal vision, the fundus was seen to be normal in the parents and maternal grandparents. Nine paternal aunts and uncles had normal vision, and twelve maternal aunts and uncles were free from defect. Two paternal first cousins and three maternal first cousins suffered from some defect in hearing. Further information can be obtained from the greatly extended pedigree of the original account. No consanguinity. Bibl. No. 301.

Fig. 141. *Usher's Case* 28. One, possibly two, cases of retinitis pigmentosa in a sibship of six. III. 2, a male, basket-maker, aged 52 (1897), had gradual failure of vision since the age of 24; in each eye there was extensive retinal pigmentation and choroidal vessels much exposed; posterior lens opacities and vitreous opacities were present in the left eye; R. V. = L. V. = perception of light; refraction was myopic. Patient had been subject to headaches and vomiting since the age of 24, he had lateral nystagmus, and venereal trouble. His sister, III. 4, was reported to have the "same sight" as his own; two sisters and two brothers had normal vision. Parents and grandparents had normal vision. No consanguinity. Bibl. No. 301.

Fig. 142. *Usher's Case* 32. A single case of retinitis pigmentosa in an only child born before the

marriage of his parents. III. 1, aged 24 (1911), a healthy farm labourer, with no history of illness except measles and whooping cough, had noticed that he was night-blind for fifteen years, he was also deaf, but not completely so. He was seen first in 1901, when *retinitis pigmentosa sine pigmento* was diagnosed, night-blindness was then demonstrated, both fields of vision were slightly contracted, and the fundus was normal, excepting a possibly too uniform colour of disc; refraction in both was myopic, 2 D. in oblique meridian, 2·5 D. in opposite meridian, corrected vision = $\frac{6}{12}$ in both. Ten years later both fundi presented the usual appearance of well-marked retinitis pigmentosa, night-blindness was troublesome, but he could read almost the smallest print in day-time. His parents were robust and had normal fundi, each had low hypermetropia. Twelve aunts and uncles, the grandparents and great-grandparents, sixty first cousins, and many more distant relatives shown in the original pedigree had normal vision. Four maternal second cousins had myopia, one paternal second cousin was mentally defective, and died aged 20. One maternal aunt, II. 9, had a normal right fundus, near the periphery of left fundus on temporal side was an area three times the size of O. D. with well-defined margin, roughly circular, in which choroidal vessels were well seen, the rest of the fundus was dark, and choroidal vessels were hardly visible. No consanguinity. Bibl. No. 301.

PLATE XII. Fig. 143. *Usher's Case* 16. A single case of retinitis pigmentosa in a sibship of six. III. 10, a farmer, aged 54 (1912), had never seen well in the dark, had "inflammation of lungs" when a boy, some bleeding of nose when young but not severe, was not subject to cold hands or feet, radial arteries normal; refraction hm. 1 D. in both eyes; R. V. with correction = $\frac{6}{36}$, L. V. with correction = $\frac{6}{60}$; light sense much diminished; both fields nearly full with symmetrical absolute ring scotoma; O. D.'s too pale; retinal arteries much narrowed; choroidal vessels exposed, though not at the periphery; retinal pigmentation fairly typical but limited to inner part of each fundus; no atrophic choroidal patches. Wassermann test negative. Parents and grandparents had good vision.

The patient's siblings were all abroad, and saw well; his seven children were all examined by the author, and had normal fundi.

Two maternal first cousins of the patient had goitre, III. 31 and 36, the former was seen, and had no exophthalmos, tremors, or rapid pulse; she had thirteen children, many of whom were examined and had normal fundi, one of them, IV. 27, was subject to epileptic fits.

Four second cousins, III. 37, 38, 49, 50, were mentally defective, also two first cousins, once removed, II. 15 and 17. Information concerning this branch of the family was given by a medical man, III. 45, who was subject to cold hands and feet and signs of early arterial degeneration; one of his sisters, III. 43, and her mother, II. 18, had cataract; one of his daughters, IV. 39, also was subject to cold hands and feet. All other members of this extensive pedigree were reported to be normal. No consanguinity. Bibl. No. 301.

Fig. 144. *Usher's Case* 36. A single case of retinitis pigmentosa in a sibship of twelve and a doubtful case in a grandchild. II. 21, female, aged 54 (1896), the youngest in a large family, had never had good sight, it had been getting worse for some years, and she was bothered by bright light; at the age of 8 she had been badly fed and was taken to an orphanage; she was found to have extensive peripheral retinal pigmentation, retinal vessels narrow, discs pale, opacities at posterior part of lens, vitreous opacity; R. V. = L. V. = $\frac{6}{60}$; fields of vision contracted to 12°, 10° at some parts. At the age of 70 (1912) she had complete cataract in both eyes with no perception of light; she was healthy and active. Her parents, I. 3 and 4, were believed to have died comparatively young. No visual defect was known in her uncle, I. 2, or his descendants, but one of his seven children and one of his grandchildren had hare-lip. Of the siblings of II. 21 four died young, II. 16 was stillborn, II. 18 had delusions and was in a lunatic asylum, his fundi were normal; II. 12, with normal vision, married a woman, II. 13, who was normal herself, but had four deaf-mute cousins; one of their eight children, III. 15, had ten children, of whom three were deaf-mutes and two twins died in infancy; six of these children were examined, and found to have normal fundi. II. 21 had three miscarriages and six children, of whom III. 36 died aged 1 day, and III. 48, aged 18 (1896), had myopia of 8 D. in both eyes, her fundi were normal except for myopic crescents; other members of the sibship and their children were free from visual defect with one exception, a daughter of III. 44. She, IV. 40, a bright girl, aged 12, made no complaint of vision; R. and L. fundi showed a few particles of pigment at periphery of retina at one point, questionable whether retinal arteries were narrowed and O. D. too pale. A few months later (1912) R. V. = $\frac{6}{24}$, with + 1 D. cyl. = $\frac{6}{9}$ partly, L. V. = $\frac{6}{18}$, with + 1 D. cyl. = $\frac{6}{12}$ partly, she had no demonstrable night-blindness, fields of vision were definitely contracted except down and in; no ring scotoma; discs just appreciably too pale, retinal arteries narrowed to a small extent, choroidal vessels exposed towards the periphery where fundus had a mottled appearance, and there was here and there a small deposit of pigment in the retina. No evidence of syphilis in the parents or any of their children.

III. 7, whose wife was in a lunatic asylum, believed that his son, IV. 4, was mentally affected, for he was morose, and had sometimes assaulted him.

No other defects were known in this pedigree. No consanguinity. Bibl. No. 301.

Fig. 145. *Usher's Case* 26. A single case of retinitis pigmentosa in a sibship of eleven. III. 16, male,

aged 14 (1911), had had gradually failing vision for four or five years, he was unable to see at dusk; had always been very healthy: four years ago he lost about a teacupful of blood after cutting his right fore-finger with an axe, the wound healed readily, but he said that after this his sight began to fail; he was fairly intelligent though somewhat slow mentally, memory good; hair very dark and stubbly, some dark hair on upper lip, forehead narrow, no deformities or bony thickenings, high palate, teeth good but irregular, no enlarged glands in neck, axillae or groins; pulse 75, regular, systolic pressure 120 mm. Hg.; hearing, smell, and speech normal; Wassermann test positive, and when repeated was again positive. His light sense was markedly defective, read $\frac{6}{60}$ in a light which gave normal eyes $\frac{6}{9}$ partly; refraction low hypermetropia, with correction R. V. = L. V. = $\frac{6}{18}$; media clear, retinal arteries much narrowed, choroidal vessels much exposed, no white atrophic spots; discs pale, with well defined edge; retinal pigmentation was present only at nasal part of R. fundus, and at nasal part and outer periphery in L. fundus: in these parts pigment was very scanty, had a moss-like arrangement, and was not very dark, in addition there was in the left eye a not very dark pepper-like mottling in some places behind the retinal vessels; the fields of vision were contracted, especially the upper halves. This boy had probably been vaccinated from arm to arm, but his mother reports that the pustule healed without trouble, and was followed by no illness.

Of the siblings of III. 16, one, III. 15, died aged 19, of pneumonia, he was reported to have had good vision and no night-blindness; III. 17—25, all had good vision and normal fundi, III. 19 had low myopia, the others low hypermetropia.

The mother, II. 18, had had no miscarriages or stillborn babies, she had good vision and normal fundi, and there was no known visual defect in her siblings or their children; one of her siblings, II. 26, was in a lunatic asylum; her parents and grandparents were reported to have had normal vision, one of her grandparents died of phthisis.

The father of III. 16 had normal fundi, he was in a lunatic asylum at the age of 18 for depression, there was no visual defect in his siblings or their children, but II. 4 died of phthisis, aged 23, and her two illegitimate children both died young, II. 6 was weak-minded and very quiet, II. 8 had a leg amputated at the knee for white swelling, II. 12, himself normal, had five normal children, and one, III. 10, who died aged 11 years, mentally weak, with large head and small body. II. 16 was in a lunatic asylum, and all his six children died young. The parents, grandparents, and great-grandparents of II. 11 were believed to have had normal vision, but his father, I. 1, had his leg amputated above the knee for white swelling. For further information concerning other normal members of the family see the author's original history and his considerably enlarged pedigree. No consanguinity. Bibl. No. 301.

Fig. 146. *Usher's Case* 20. A single case of retinitis pigmentosa associated with lamellar cataracts in a boy, III. 13, aged 17 (1908). He was well nourished, never had fits, was fidgety, teeth and palate normal, had mumps and measles when at school; at the age of 4 years he fell against a broken pail and cut bridge of nose, he was said to have lost much blood, but the evidence was not convincing; defective vision was noticed at the age of six or seven years, and had been getting worse. Typical symmetrical lamellar cataracts were removed by curette extraction in 1908 and 1909; after operation in each the course was uneventful; retinitis pigmentosa was first detected after removal of lenses. In each eye there was marked retinal pigmentation, with moss-like character, all over periphery of fundus; retinal arteries not markedly contracted; O. D. a good colour; night-blindness; fields of vision markedly contracted; refraction before operation R. my. 2·5 D., V. with correction = $\frac{6}{6\,0}$, L. emm. V. = $\frac{6}{6\,0}$; after operation R. hm. 11 D., V. with correction = $\frac{6}{3\,6}$, L. hm. 10 D., V. with correction = $\frac{6}{6\,0}$. In 1912 central vision and refraction were unaltered, in dim light allowing a normal eye to read $\frac{6}{12}$, he could only read $\frac{4}{6\,0}$; right field of vision was reduced to 10°, left field was rather less; retinal pigment had increased. Wassermann test negative.

II. 6, aged 54, mother of III. 13, had media clear and fundus normal in each eye; one of her two brothers, II. 7, had R. my. approximately 5 D., L. traumatic cataract; one of her five sisters held things close to her, but was not night-blind. The maternal grandparents, I. 3 and 4, had good vision, as also had the parents of I. 4 (not given in pedigree). II. 5, aged 64, father of III. 13, had media clear and fundi normal; one of his five brothers, II. 3, had a R. senile cataract, his other four brothers and four sisters, with their descendants, had normal vision; the paternal grandparents had normal vision.

Of the siblings of III. 13, III. 17 was stillborn; III. 18 died, aged 2 months, and the living eleven had normal vision. Twelve nieces and nephews of the patient also had good vision.

The original pedigree gives information of 51 first cousins and other more distant relatives. The author examined 37 individuals. No consanguinity. Bibl. No. 301.

PLATE XIII. Fig. 147. *Usher's Case* 33. A single case of retinitis pigmentosa in a sibship of twelve, with a doubtful case in the next generation, in which changes were limited to the macular area, in a large pedigree otherwise remarkably free from defect. IV. 29, female, aged 39 (1908), had had difficulty in seeing at a distance for two years, and slight frontal headaches; the retinal arteries were narrowed, discs a little pale; well marked retinal pigmentation was present at inner part of fundus between the periphery and the disc; media clear; fields of vision full; absolute symmetrical ring scotoma; refraction, R. hm. 0·5 D.

in oblique meridian, my. 1·5 D. in opposite meridian, corrected V. = $\frac{6}{9}$, L. emm. in oblique meridian, my. 2 D. in opposite meridian, corrected V. = $\frac{6}{9}$; no complaint of night-blindness. The patient was liable to indigestion, and had a history of typhus fever at the age of 12, also of inflammation of the bladder and congestion of kidneys; urine was free from albumen and sugar. She had three unaffected daughters, the eldest of whom was aged 19. Five of her siblings died in infancy, IV. 25 died aged 37, of "apoplexy," IV. 26 died aged 21, of typhus, IV. 28 died aged 15, of "abscess," IV. 35 was at sea, IV. 36 was a nurse.

III. 11, father to IV. 29, had normal fundi; one of his four siblings, III. 16, had senile cataract; his mother, II. 10, was blind for six years before her death at the age of 66; one of his first cousins once removed, IV. 1, male, had a large patch of choroido-retinitis at periphery of nasal half of fundus with dense black pigment, some in front of retinal vessels, and almost complete choroidal atrophy, discs were normal and retinal arteries of normal size. All other ancestry or descendants of III. 11 were believed to have normal vision with the exception of his great niece, V. 12, aged 31 (1908), who had had defective vision as long as she could remember; discs were a little pale, retinal vessels perhaps a little narrowed; there was retinal pigmentation limited to the macular region and in branched forms coarser than is usual in retinitis pigmentosa; choroidal vessels seen indistinctly in pigmented area; light sense was markedly defective; fields of vision full, paracentral absolute scotoma below fixation point; refraction my. R. and L. 1 D., V. = finger counting at 3 feet in each; Wassermann test positive; in 1908 was in hospital with pelvic cellulitis, "no history of syphilis"; her first child died aged 4 months, the next three children had normal fundi, VI. 5 represents two miscarriages. The only sibling of V. 12 had normal fundi, her mother, IV. 13, died, aged 27, of "decline," her father, IV. 12, died of kidney disease.

III. 35, the mother of IV. 29, had good vision, she was the daughter of first cousins; there was no known visual defect in her relatives. Further information of normal members may be obtained from the author's account of the family. Consanguinity. Bibl. No. 301.

Fig. 148. *Usher's Case* 11. Two cases of retinitis pigmentosa associated with deafness, and two cases of congenital nystagmus in a sibship of nine. III. 12, an unmarried female, aged 44 (1906), had had gradual failure of vision since night-blindness was first noticed at the age of 20 or later; she had no defect at school age when she had sometimes to walk home in the dark along a country road; her eyes were painful and watered; she had no history of illness or severe bleeding, but had a fright at the age of 20; she was very deaf. R. V. = $\frac{6}{24}$, L. V. = $\frac{6}{36}$; posterior cortical lens opacities were present; discs were pale, retinal vessels markedly contracted, choroidal vessels much exposed; there was much retinal pigmentation at the periphery of each fundus; fields of vision contracted to from 10° to 20°. Seen six years later the condition of fundus was unchanged; Wassermann test negative. Her brother, III. 8, an unmarried farmer, aged 57 (1912), was very deaf, and had had chronic blepharitis since measles; at the age of 16 he had a discharge from the clavicle, and fragments of bone came away; no bleedings; he had marked night-blindness which had been noticed at an age much earlier than in his sister's case; he reported that he heard and saw well before he had measles. Refraction was myopic, R. V. = L. V. = 1 J.; nystagmus was present; posterior cortical lens opacities; discs were pale, and retinal arteries narrow; much retinal pigmentation was present at the periphery of the retina. III. 11, a twin, aged 53 (1912), was not night-blind, could read ordinary print easily, and had normal fundi, but he had a constant lateral nystagmus in both eyes, which had been "present from birth"; his irides were green, yellow in parts, and his hair was yellow. His twin brother, III. 10, died aged 14 months. III. 5, with good vision and no night-blindness, had constant nystagmus present since birth. Two sisters, III. 7 and III. 13, had normal fundi, no deafness and no nystagmus. III. 3 died in infancy; III. 9 died unmarried. Two of this sibship had children, all of whom saw well. An illegitimate half-brother, III. 2, was normal, his nine children and two grandchildren saw well.

Both parents, II. 8 and 9, had good vision; the father's siblings nearly all lived to be over 70; a sister, II. 3, had cataract, the others with their twenty children and about twenty grandchildren had no known defects of vision, but two of the children, nephews to II. 8, died of phthisis. The mother's six siblings had normal vision; one of them had four children with normal vision, of whom one died in a lunatic asylum.

The maternal grandparents had normal vision, and were unrelated, the paternal grandparents, I. 1 and 2, had good vision, and were first cousins. A brother of I. 1 had two children, whose vision became defective, one of them had an operation on his eyes, and the other became blind late in life; a child of the first of these "screws his eyes up." A paternal second cousin of the sibship III. 3—13 was in a lunatic asylum for a few months at the age of 22.

Three of the great-grandparents were reported to have normal vision. For further information about normal members see the author's original history and enlarged pedigree. Consanguinity. Bibl. No. 301.

Fig. 149. *Usher's Case* 4. Four cases of retinitis pigmentosa in one sibship, the offspring of first cousins. III. 5, aged 57 (1912), saw sufficiently well for schooling, but since then his vision had gradually failed until he became quite blind, he had been night-blind; R. V. = L. V. = no perception of light; retinal pigmentation could be seen in the right eye, the left fundus was not visible owing to complete cataract;

he had congenital coloboma of iris in the left eye only; Wassermann test negative; he and all his siblings, except III. 7, had scarlet fever in childhood. III. 6, aged 41 (1898), had never been strong, she was night-blind, and her vision gradually failed, she saw well enough for schooling, but was blind at the time of examination; slow vertical nystagmus, myopia, R. V. = L. V. = no perception of light; retinal vessels, especially the arteries, were extremely narrow; there was much pigmentation at the periphery of retina of a moss-like pattern: the discs were of a pale yellow-red colour, with the edge not sharply defined. III. 7, aged 37 (1897), had "gastric fever" at the age of 13, but her vision began to fail before then, and she was almost blind at the time of examination; R. V. = L. V. = perception of light; she had slow lateral nystagmus, posterior cortical lens opacities; choroidal vessels much exposed, and retinal vessels very narrow; very extensive retinal pigmentation, reaching nearly to the discs. Seen again in 1912, she had no perception of light, and much lens opacity. III. 8 had R. V. = L. V. = no perception of light when seen in 1912, her vision had gradually failed; she had much lens opacity and details of discs, and retinal vessels could not be seen, but typical retinal pigmentation was visible; Wassermann test negative. Of the unaffected members of the sibship, III. 2, a healthy farmer, with normal fundi, had nine normal children, the first of whom was illegitimate, and five normal grandchildren; one of his nine children, however, IV. 7, aged 18, said on being questioned that for two years she had found some difficulty in seeing at dusk, she had never told this to her family, and they had never noticed any difficulty; she was peculiar, and possibly neurotic; the author examined her on two occasions, and found no diminution of light sense, no contraction of fields (perimeter not available) or ring scotoma, discs and retinal vessels were normal, but there was a yellowish dappled appearance at parts of the periphery of the retina, and at least one piece of retinal pigment visible. III. 4, died, aged 8 years, she saw and heard well. III. 9, also her children and grandchildren, had normal vision. III. 11 represents four miscarriages, the position of which in the sibship was unknown.

The parents of this sibship lived to old age and had good vision, as also had their parents and grandparents.

The mother's four siblings, with the descendants of the only one of them who had children, had normal vision; one of her sisters, II. 11, had normal illegitimate twins by her first cousin, II. 6, the brother of II. 3.

The father's seven siblings, with their descendants, had normal vision, but one of his nephews had a violent temper which was attributed to insanity, and later he became alcoholic.

A great-uncle, I. 5, was a "character," went about in old-fashioned costume, and was regarded as eccentric. The original pedigree shows a large number of his descendants, none of whom had defective vision, but one granddaughter had exophthalmic goitre, and she had a hysterical daughter, one great-grandson was mentally defective, and one was epileptic.

The original pedigree is greatly extended, and is described in great detail by the author; the only further cases of eye defect in the history were in a branch of distant connection where there were fundus changes not associated with night-blindness, and believed by the author to be due to high myopia. Consanguinity. Bibl. No. 301.

Fig. 150. *Usher's Case* 13. Four cases of retinitis pigmentosa, associated with deaf-mutism, in a sibship of seven. III. 2, aged about 17 (1911), was a deaf-mute with marked night-blindness, his defect of vision was not noticed until the age of 7 or 8 years; R. V. = L. V. = 1 J. in a good light; the discs were pale, the retinal vessels contracted, and there was a typical appearance of retinitis pigmentosa in each fundus; fields of vision were contracted. III. 4, male, aged about 15 (1911), was a deaf-mute, with night-blindness, which was first noticed at the age of 7 years; fundus changes were similar to those of III. 2. III. 6, aged 9 (1911), a mentally weak deaf-mute, was considered to be night-blind by those in charge at an institution for the deaf and dumb because in a dim light she knocked against objects which other children would avoid, but her mental condition was such that it was not possible to demonstrate that she was night-blind; the retinal vessels were narrow, the discs pale, choroidal vessels exposed; there was some yellowish mottling towards the periphery of the fundus, but no moss-like pigmentation; refraction hm. 2 D. in vertical meridian, 6 D. in horizontal meridian for each eye; Wassermann test negative. III. 7, aged 7 (1911), was a deaf-mute, and was believed to have not marked night-blindness; there was much yellowish mottling towards the periphery of the fundus behind the retinal vessels, and much pepper-like pigmentation of the fundus with two or three moss-like deposits at the periphery in front of the retinal vessels; refraction hm. R. 2 D. in vertical, 3·5 D. in horizontal meridian, L. 2 D. in vertical 5 D., in horizontal meridian; Wassermann test negative. None of these four children had a history of illness or bleeding; of their normal siblings III. 1, aged 18, had no deafness or myopia, her right fundus showed a dense white band extending from the inner edge of the disc to beyond its centre, otherwise both fundi were normal. III. 3 had a normal fundus. III. 5 died in infancy.

The mother of this sibship was always delicate, she died aged 44, of phthisis; she was third born in a sibship of thirteen, two of whom died in infancy, also one of her sisters and one brother died of phthisis; there were no defects of vision in her parents, I. 3 and 4, her grandparents, or their descendants other than those recorded above. The father, II. 3, was an intelligent robust farmer, with a normal fundus, his

three siblings, his parents and his grandparents with their descendants all had normal vision except the sibship III. 1—7.

Thirty-one first cousins and other more distant relations to the sibship III. 1—7 are shown on the original pedigree with no defects of vision. No consanguinity. Bibl. No. 301.

Fig. 151. *Usher's Case* 15. A single case of retinitis pigmentosa in a sibship of four. III. 2, male, aged 14 (1896), a farm servant, did not see well at night; at the age of $2\frac{1}{2}$ years he had been ill for six weeks with "inflammation of brain," and his father believed that his sight had been defective since; his nose bled daily when at school; he did not suffer from cold hands and feet; he was intelligent and healthy, with no evidence of syphilis. R. and L. well-marked retinal pigmentation with moss-like character, an unpigmented part of retina was present peripherally to the pigmented area at temporal and nasal sides, but not above or below; choroidal vessels exposed. O. D., of uniform reddish colour, with blurred edges; retinal vessels narrowed; posterior cortical lens opacities; refraction hm. R. 2 D. in oblique meridian, 4·5 D. in opposite meridian, corrected V. $= \frac{6}{12}$, L. 1·5 D. in horizontal meridian, emm. in vertical meridian, corrected V. $= \frac{6}{9}$; fields of vision were contracted. In 1912, R. V. $= \frac{6}{24}$, L. V. $= \frac{6}{18}$, not improved by glasses; O. D. waxy, moss-like retinal pigmentation not extending to central region; retinal vessels very narrow; no white patches in choroid; Wassermann negative. His father, II. 6, was illegitimate, and had normal fundi; the paternal grandfather went abroad and was not known, but the paternal grandmother and the six half siblings of the father had normal vision. His mother, II. 10, and her parents had normal vision; of her siblings, II. 11 died young of diphtheria, five had good vision, and II. 8, female aged 61, had difficulty in seeing at dusk, but fields of vision were full, and she had no ring scotoma; she had my. 0·75 D. R. and L. V. R. = V. L. $= \frac{6}{12}$ with correction, in dim light, giving $\frac{6}{18}$ to normal eyes, she did not read $\frac{6}{60}$; R. and L. O. D., a good colour, retinal arteries not contracted; at macula there was an area 2 O. D. in size, mottled with small yellowish spots which were interspersed and covered by small black pigment spots; in R. white crescent of choroidal atrophy next onter and lower edge of O. D., and at lower part of fundus two large oval yellowish spots with well-defined and pigmented margins (probably syphilitic); she had had two miscarriages, two children who died in infancy and two who lived; Wassermann positive.

The original more extensive pedigree shows six great-grandparents of III. 2, with normal vision, also thirteen maternal cousins and many more distant relations. The mother, II. 10, had an uncle and two first cousins who showed some degree of mental defect.

Of the siblings of III. 2, a sister, III. 1, had high hm. astigmatism with normal fundi, two brothers had normal vision. No consanguinity. Bibl. No. 301.

Fig. 152. *Usher's Case* 12. A single case of atypical retinitis pigmentosa in a sibship of five. III. 2, aged 6 years (1911), had uniform pallor of discs, physiological cup not filled in, retinal vessels very narrow and all over the periphery of the fundus were numerous small black pigment specks and much delicate branched pigment in the retina; there was little, if any, coarse moss-like pigment, and no circular patches of choroidal atrophy; in some large areas at the periphery the choroidal vessels showed more than elsewhere; no lens opacity; refraction hm., R. 3·5 D. in oblique, 6·5 D. in opposite meridian, L. 3 D. in oblique, 6·5 D. in opposite meridian; when she dropped small things her mother said she did not see them, yet in a badly lit room she seemed to have little difficulty in finding things on the floor. At the age of 17 months she did not see well, and there was constant lateral nystagmus with no gross fundus lesion, a year or so later ill-defined changes were present at the macula with pepper-like pigmentation and choroid paler at one spot; Wassermann test negative. Her four siblings had normal fundi, though the examination was unsatisfactory in the case of the youngest.

The mother, II. 8, had myopic astigmatism, no retinitis pigmentosa; her siblings and their seventeen children had no defects of vision; her parents, also their siblings, her grandparents and one great-grandparent had normal vision.

The father, II. 2, had a normal fundus, he had no siblings, his parents and grandparents had good vision; his half-aunt, I. 2, became blind after the age of 50; the cause was unknown, but the history was not suggestive of retinitis pigmentosa; she had one son, II. 1, who at the age of 45 had absolute glaucoma in each eye.

For further information concerning more distant relatives see the author's account of the case and his extended pedigree. No consanguinity. Bibl. No. 301.

PLATE XIV. Fig. 153. *Usher's Case* 24. An isolated case of retinitis pigmentosa in a female who had a positive Wassermann reaction; IV. 5, aged 24 (1898), had suffered from night-blindness and difficulty in reading and sewing for 12 years. Examination showed R. and L. marked retinal pigmentation at periphery of fundus except at outer part, no white patches; the discs were a dirty reddish colour, paler than normal; retinal vessels, especially arteries, very narrow; at nasal part of left fundus, between the disc and the pigmented area, was a speckled, pepper-like distribution of pigment; refraction my. R. 2 D., V. with correction $= \frac{6}{12}$, L. 1·75 D., V. with correction $= \frac{6}{12}$; fields of vision peripherally contracted, left to within 20°, right at temporal part to 30°, at other parts to within 20°. Seen again in 1907 with R. and L. small posterior cortical cataracts; discs waxy; retinal pigment approaching central region of fundus, but not

involving macula, R. V. with correction = $\frac{6}{12}$, L. V. with correction = $\frac{6}{18}$; R. field more contracted, L. field as before; she was mentally slow, and had no issue from her three marriages; she was delicate and an only child; when six weeks old her mother had "spotted (black) typhus fever." Her mother, III. 3, aged 65 (1911), was quite blind from primary glaucoma, she was an only child, and married her cousin, III. 6, the father of IV. 5; she had no children by her second husband, but had three illegitimate children by III. 2 and III. 4, all of whom had normal vision.

The father of IV. 5 was also the offspring of first cousins; his sister, III. 7, had retinal haemorrhages, but no retinitis pigmentosa, she also married her first cousin, and had five children with normal vision; another sister, III. 8, had a son with hydrocephalus and bilateral optic atrophy, and three children with normal vision; a brother, III. 10, had three children with normal vision. Other members of Gen. IV. had normal vision, but IV. 37 was in a lunatic asylum.

In Gen. V. one individual, V. 14, aged 4, daughter of one of the illegitimate children of III. 3, was an imbecile, did not speak, and had to be fed; she had nystagmus and gross choroido-retinitis in each eye. V. 18 had corneal opacities; V. 20 had a congenital crescent in left fundus, right eye myopic; V. 21 was mentally defective.

The author examined fifty-four members of this pedigree, and gives further information in his description of it. Consanguinity. Bibl. No. 301.

Fig. 154. *Usher's Case* 2. One case of retinitis pigmentosa in a sibship of three, the offspring of first cousins. III. 4, aged 37 (1910), was badly nourished and had never been strong, but there was no history of definite illness, and her face and teeth were not suggestive of inherited syphilis; she was very deaf, and though married, had no children; Wassermann test negative. Her vision was defective at the age of 16, and she had great difficulty in getting about in a dim light; in both eyes there was much retinal pigmentation; the discs were pale, retinal arteries narrow; posterior lens opacities were present; night-blindness was marked; fields of vision were contracted to about 10°; refraction R. simple myopic astigmatism of 3 D., corrected V. = $\frac{6}{24}$, L. myopia of 2 D. in horizontal, 4 D. in vertical meridian, corrected V. = $\frac{6}{18}$.

The mother of III. 4 died, aged 54, of cancer, she had eight siblings, of whom three died young; one, II. 6, had gross symmetrical choroido-retinitis and night-blindness, probably syphilitic, the remaining four, with their children and grandchildren, had good vision; the parents and grandparents were not known to have had any defect of vision.

The father of III. 4 and all his three siblings died of phthisis, neither they nor their parents were known to have had any defect of vision.

The two siblings of III. 4, and the five children of one of them, saw well.

The author's pedigree shows twenty-seven first cousins to III. 4, and other more distant relatives, who were believed to see well. Consanguinity. Bibl. No. 301.

Fig. 155. *Usher's Case* 40. An isolated case of retinitis pigmentosa in a male in a childship of seven. III. 13 was a gamekeeper, aged 43 (1894), his vision had been failing rapidly in both eyes for three months, he could see best in dim light, R. V. = $\frac{6}{18}$, L. V. = $\frac{6}{24}$, not improved by glasses; fields of vision were full with absolute ring scotoma complete in both though very narrow at upper nasal part in R.; optic discs waxy; retinal vessels diminished; moss arrangement of pigment in retina between disc and periphery, but there was no pigment immediately around the disc or at extreme periphery; patient unable to shoot ground game, but could shoot birds. Seventeen years later (1912) he was working in a mill as timekeeper, and could still read 1 J. with each eye readily; no history of syphilis; had "gastric fever" at age of 14; was badly shot in 1876, had 78 pellets in him; up to the age of 20 was subject to severe nose bleeding; did not bruise readily; no night-blindness; fields of vision taken with 10 mm. square of white paper on end of a stick had an absolute ring scotoma below and at nasal part, but not above or in temporal parts, where fields were contracted to perhaps 10° or 15°; retinal arteries were narrow; discs pale; choroidal vessels exposed; retinal pigment extended nearly to discs. The patient reported that his parents, grandparents, two brothers, four sisters, and his twelve children had all had good vision. The author examined the fundus of six children of the patient, and found all normal. The pedigree shows a large number of nieces and nephews, also aunts, uncles, and cousins apparently free from all eye trouble, and showing no other inheritable disease except in the case of two nephews, IV. 7 and 10, who died of phthisis. No consanguinity. Bibl. No. 301.

Fig. 156. *Usher's Case.* Six males affected with retinitis pigmentosa in four generations. I. 3 was invalided from the army as a young man for "moon-blindness," and was told it would get worse; he could see well in the day at this time, but not in the evening; he got steadily worse, was quite blind at the age of 50, and died aged 70. I. 1, 2 and 4 had good sight. II. 1 and 5 had good sight. Of their eight children III. 3 died in infancy; III. 4 died aged 14; III. 5, aged 40, had good sight, and his three children also had normal vision. III. 7, aged 38, had typical advanced retinitis pigmentosa, his four sons and his daughter, who had died recently, had normal vision. III. 9, aged 36, had typical advanced retinitis pigmentosa, his only son had normal vision. III. 11, aged 34, with typical retinitis pigmentosa, was married but had no children. III. 13 and 14 had normal vision, but the child of one of them, III. 14, seen by the author at a later date (Bibl. No. 301), then aged 8, had typical retinitis pigmentosa.

III. 17, first cousin to the previous three cases, aged 50, was nearly blind from retinitis pigmentosa; he was a drinker; by his first wife there were no children; by his second wife he had five or six children, of whom one or two had bad sight by day as well as by night. No consanguinity recorded. Bibl. No. 263, p. CLIII.

Fig. 157. *Usher's Case* 1. A single case of retinitis pigmentosa in a sibship of two. III. 3, aged 30 (1911), a widow, had never seen so well as others in a dim light; she was never strong, but had no history of illness or bleedings; her discs were pale and waxy, her retinal arteries narrow; there was moss-like retinal pigmentation visible chiefly at the (not extreme) periphery; choroidal vessels were conspicuous; posterior cortical opacities of the lenses; refraction was low hypermetropia, corrected V. = $\frac{6}{12}$ partly; she was night-blind; fields of vision much contracted; Wassermann test negative. She had been examined by the author thirteen years previously, the visual fields had contracted considerably in the interval, the defect in light sense was unchanged. IV. 3, the only child of III. 3, had a normal fundus. III. 2, the only sibling of III. 3, saw well, and her only child IV. 1 had a normal fundus.

II. 9, mother of III. 3, had a normal fundus; the father, II. 5, had good vision and no night-blindness. The grandparents and five great-grandparents, with all their descendants except III. 3, were free from any defect of vision so far as was known.

Two maternal first cousins to III. 3, and one paternal first cousin, died of phthisis; one maternal first cousin once removed "went wrong in his mind," and was in an asylum.

The original greatly extended pedigree shows twenty-seven first cousins and a large number of more distant relatives of the patient III. 3, all of whom were believed to be free from defect of sight or hearing or other inheritable defect, except the cases mentioned above. No consanguinity. Bibl. No. 301.

Fig. 158. *Usher's Case* 17. Two cases of retinitis pigmentosa in a sibship of nine. III. 1, male, unmarried, aged 24 (1911), the illegitimate son of II. 8 and 10 before their marriage, was a healthy-looking farm servant; night-blindness noticed when he left school, aged 14; had no illnesses, and had incomplete deafness. He was examined in 1902, and again in 1911, when the condition had progressed; at the latter date he had very extensive moss-like pigmentation at the periphery of the fundus: retinal arteries much narrowed; O. D. pale, with edge not well defined; posterior lens opacities; R. V. = L. V. = $\frac{6}{12}$; hm. 0·5 D. in each; in dim light that gave $\frac{6}{9}$ to a normal person he could only read $\frac{6}{60}$; fields of vision contracted to 18°, except at a point on horizontal line in outer part of fields where it reached 22°; no ring scotoma; hearing, right ear does not hear a watch on contact, left ear hears watch only on contact; smell normal; Wassermann test negative; no history of illness or bleedings.

III. 5, female, unmarried, aged 18 (1911), had always been deaf like her brother, she was night-blind, and had had no illnesses or bleedings; on examination some vitreous opacities were found; retinal vessels narrowed; discs showed no marked pallor, but edges were hazy; at periphery of fundus were yellow-white spots and some pepper-like dots; in R. only two spots of pigment were visible, one at outer, the other at inner periphery, in L. two similar black spots were down out at periphery; no white atrophic spots; choroidal vessels exposed; refraction R. my. 3·5 D. in oblique and emm. in opposite meridian V. with correction = $\frac{6}{12}$; L. my. 1 D. in oblique, 3·5 D. in opposite meridian, V. with correction = $\frac{6}{12}$; with correction in a dim light that gives a normal person $\frac{6}{12}$ she gets $\frac{6}{36}$; fields contracted most markedly above, in R. is an incomplete narrow ring scotoma; hearing as for III. 1; smell normal; Wassermann test negative. III. 3, 6, 8 and 9 had normal fundi; III. 2 and 4 had normal vision; III. 7 died aged 3, of "water in head."

The mother, II. 10, died of pneumonia, but had normal vision; her four siblings apparently also had normal vision.

The father, II. 8, had a normal fundus; his sister, II. 9, had "water in head," difficulty in walking, was deformed and probably silly; II. 7 died aged 2; II. 3 died aged 25 in a lunatic asylum, had fits; II. 1 died in infancy; II. 2 had a normal fundus; II. 4 and 6 had good sight. The paternal grandparents I. 1 and 2 were related, but not first cousins, they lived to old age and saw well; one sibling of I. 1 was deformed, and two siblings of I. 2 were probably myopic. The four parents of I. 1 and I. 2 were reported to have seen well. The maternal grandparents I. 3 and I. 4 saw well, and there was no reported defect in their siblings or in the parents of I. 4. For further information see the original greatly extended pedigree, which shows thirty-three first cousins to the sibship of III. 1 to 9, and a large number of more distant relatives, all believed to be free from hereditary defect. No consanguinity. Bibl. No. 301.

PLATE XV. Fig. 159. *Usher's Case* 27. Three cases of retinitis pigmentosa in a sibship of seven. III. 24, a farmer, aged 37 (1899), had scarlet fever in childhood, but no history of syphilis or other illness, and no severe bleedings; Wassermann test positive; the discs were pale, the retinal vessels much narrowed; retinal pigmentation was visible mostly at the periphery and in the form of fine granules; choroidal vessels much exposed; a few circular grey spots, one-sixth diameter of O. D., were seen in lower part of fundus, with choroidal vessels crossing them; refraction emm; R. V. = L. V. = $\frac{6}{24}$; fields of vision contracted to 10°. Thirteen years later his vision was reduced to perception of light in each; posterior cortical lens opacities were present with moss-like retinal pigmentation except at the macula. He had records of hospital notes given him at the age of 27, when R. V. = L. V. = $\frac{6}{9}$, and no pigment was seen in either eye.

III. 16, a farmer aged 67 (1912), was mentally keen, but not robust in appearance; no history of illness, unless possibly scarlet fever, and no bleedings; he had posterior cortical cataracts; discs were waxy, retinal vessels very narrow, choroidal vessels much exposed; moss-like retinal pigmentation was visible except at the macula; R. V. = L. V. = no perception of light, he had been quite blind for 30 years; refraction low hypermetropia; he thought the onset of his visual defect was between the ages of 20 and 30. III. 14 was abroad, he was quite blind, and was believed to be affected in the same way as his brothers; his failure of vision was first noticed about the age of 30 and from that time gradually progressed.

The parents were first cousins, they and their parents had good vision.

Of the normal siblings of the affected brothers, III. 17 died of typhoid, she had three normal children; III. 19 died aged 23 of "gastric fever"; III. 20 died of "haemorrhage," her first six children died in infancy, and the remaining four reached adult life to die of typhoid; III. 22 died aged 23 of "brain fever."

All the affected members had children, six of whom were examined and showed no signs of retinitis pigmentosa, one daughter of III. 24 and one son of III. 16 were myopic.

A sister of the father II. 8 married her first cousin, a brother of the mother II. 9, and had three children, III. 9—11, of whom III. 9 was mental and shy and refused examination, all had good vision and hearing.

IV. 31, first cousin once removed to the affected sibship, had always been bed-ridden, and had defective hearing; there was no information concerning his vision. Nineteen first cousins and many more distant relatives seen in the pedigree were free from any known defect. Consanguinity. Bibl. No. 301.

Fig. 160. *Usher's Case* 31. A single case of retinitis pigmentosa in a sibship of thirteen. III. 8, aged 28 (1911), complained of defective vision especially in a dim light, her sight had been failing for 13 years, she had frontal headaches and felt tired; she had an abscess in her leg two years before, and diphtheria at the age of 26, had frequent anaemia since the age of 18; R. V. = finger counting at 10 inches, L. V. = hand movements at 2 metres; night-blindness not very marked; discs were a homogeneous dirty red colour, retinal vessels very narrow, choroidal vessels much exposed; retinal pigmentation was only visible at the extreme periphery, it was moss-like and in some places pepper-like; fields of vision were contracted to within 10°. III. 14 died in infancy, the other siblings of III. 8 and the twelve children of two of them were healthy and saw well.

The father, II. 3, died aged 67, he had a weak heart; he, his parents, one of his grandparents, and their descendants were free from any defect of vision. The mother, II. 8, had normal fundi and was healthy; her parents, two grandparents, and their descendants, were free from visual defect, but one of her nine siblings, a sister, II. 9, was a deaf-mute with normal fundi, and one of her nieces (see the original pedigree) was mentally defective and deformed.

Fifty-three normal first cousins and many more distant relatives are shown in the author's original pedigree. No consanguinity. Bibl. No. 301.

Fig. 161. *Usher's Case* 8. Three cases of retinitis pigmentosa in a sibship of eleven. III. 8, aged 19 (1902), complained of failing vision and of night-blindness which had been first noticed by his mother when he was aged 10; he had occasional aching in the temporal regions; refraction myopic, R. 2 D., corrected V. = $\frac{6}{18}$, L. 1·5 D., corrected V. = $\frac{6}{12}$; fields of vision were contracted to 12°; pupils were small, equal in size, and reacted sluggishly to light; the discs were a fairly good colour with well-defined edge, the retinal arteries were narrowed, and typical retinal pigmentation was present; a few vitreous opacities were present; his hearing was defective, the right ear heard nothing, the left ear heard a watch on contact only; there was some defect in his speech also, but in other respects he appeared to be normal, and was of a robust physique; Wassermann test negative, and no history of illness. Seen again seven years later, his vision was worse and the condition had progressed. III. 3, a stonecutter, aged 25 (1902), was strong and intelligent and had no history of illness, but he was rather deaf, had some difficulty with his speech, and was night-blind; he was in Canada and reported that his vision was getting worse; notes of his fundus and fields could not be found. He was married, but had no children. III. 10, aged 24 (1910), was somewhat deaf and night-blind, she also had some difficulty in speaking; her retinal arteries were narrowed, her discs were pale, but not markedly so; fields of vision were contracted; vitreous opacities were present in the right eye; retinal pigmentation was typical; she had an illegitimate boy, IV. 9, who apparently had normal vision as an infant. Of the normal siblings, III. 2 was an illegitimate daughter of II. 11 by a different father; she had four sons with normal fundi. III. 4, III. 6, III. 9, and III. 12 to 15 had normal fundi, and no night-blindness. III. 16 died aged 12 months of whooping cough and teething. The three children of III. 4, and three of the four children of III. 6, had normal fundi; IV. 5 died aged 14 months.

The mother, II. 11, aged 56 (1910), had no night-blindness or contraction of fields; her vision was perfect, but at the lower periphery of the left fundus there were two or three patches of superficial choroidal atrophy with well-defined edges; there was no known defect of vision in her eight siblings, her parents or grandparents, or their descendants. The father, II. 5, aged 53 (1910), had normal fundi, several of his eleven siblings died young, the seven survivors had normal fundi or good vision; his father, I. 1, died

aged 75 quite blind, his sight failed gradually in adult life, there was no history of night-blindness, but he had had two operations for cataract. The parents of I. 1 had normal vision; his maternal grandmother died aged 102 when she had been blind for two years. I. 6 was at one time in a lunatic asylum; I. 7 was in a lunatic asylum for a number of years.

A sister of II. 5 married a brother of II. 11, and had two daughters with normal fundi.

The author's greatly enlarged pedigree shows sixty-three first cousins to the affected sibship all believed to have normal vision, as well as a considerable number of more distant relatives. No consanguinity. Bibl. No. 301.

Fig. 162. *Usher's Case* 23. Three cases of retinitis pigmentosa and one case of vacillating ring scotomata in a sibship of four. IV. 1, aged 47 (1910), was deaf, had very defective vision, and was night-blind; in 1913 there was some lens opacity, the discs were pale and waxy, the retinal vessels thread-like, the choroidal vessels much exposed, and much retinal pigmentation was visible towards the periphery; his refraction was myopic, 3 D. in each, corrected V. = $\frac{6}{24}$ in each; night-blindness was very marked; Wassermann test negative. IV. 3, aged 39 (1910), was deaf, and had marked night-blindness; he had posterior cortical cataracts, fields of vision were much contracted, and his fundus showed changes typical of retinitis pigmentosa. IV. 4, aged 34 (1910), was deaf and had defective vision, which was gradually getting worse; R. V. = L. V. = hand movements at 5 metres; pupils were equal, and reacted sluggishly to light; he had posterior cortical cataracts and retinal pigmentation, which was most marked midway between the optic disc and the periphery, some of the pigment was arranged in circles or round patches like choroidal pigmentation; retinal arteries were very narrow, and fields of vision were reduced to less than 5°. The defect of vision in each of the three brothers had been noticed as soon as they could walk. IV. 2, aged 45 (1910), reported that "nothing was thought about his sight," although his parents knew that it was not right; he was examined because his brothers had retinitis pigmentosa, and was found to have some night-blindness, some contraction of visual fields, some defect of vision, V. with correction for low hypermetropia was $\frac{6}{9}$ for each, and he had an absolute complete ring scotoma in the left field; the case was examined repeatedly at varying intervals, and the scotoma was sometimes present, sometimes absent in one or both eyes, it was sometimes complete and sometimes partial; the fundus was normal in all respects. The patient had Raynaud's disease, and was subject to migraine-like attacks, and the author was of the opinion that the source of the transient scotomata was probably vascular; he describes the case with its repeated examinations in considerable detail.

The parents of this sibship were first cousins once removed; the mother, III. 5, died aged 62; at the age of 35 she was in bed for two years with "paralysis of voice, one side of body paralysed, headaches and vomiting," vision became affected at that time and gradually got worse; quite blind in one eye at the time of death, according to the report of her relatives. There were no defects of vision known in the eleven siblings of III. 5 nor in their children, grandchildren, or great-grandchildren, except in the case of one of the five children of III. 8, who had low myopia, and one of the children of III. 7, who never saw well, but was not night-blind. The parents of III. 5 saw well. The father, III. 2, had normal fundi; his six siblings and their children, grandchildren, and great-grandchildren, had normal vision, though one sibling, III. 1, had lens opacities at the age of 73. The father and paternal grandparents of III. 2 saw well; his mother, II. 3, had cataract.

The author shows more than eighty-three first cousins of the affected sibship with no symptoms of retinitis pigmentosa, as well as many more distant relatives not included in our abridged pedigree. Consanguinity. Bibl. No. 301.

Fig. 163. *Usher's Case* 39. A single case of retinitis pigmentosa in a sibship of six. III. 6, aged 27 (1907), had always had defective vision, but it had been worse the last twelve months; she reported that she had been night-blind as long as she could remember, but her aunt said it had not been noticed until she was aged 14; she had a history of anaemia two years previously, and of typhoid fever at the age of 6; she had well-marked retinitis pigmentosa, her discs were pale, retinal vessels small, fields of vision contracted to 10°; she had posterior cortical cataract; refraction was myopic, R. 1·5 D., corrected V. = $\frac{6}{36}$, L. 2·5 D., corrected V. = $\frac{6}{18}$. The parents saw well and were unrelated; when the mother, II. 10, was pregnant with III. 6, her youngest child, III. 5, was ailing, became totally blind, and died aged 2, "the doctor stating that had she lived it would have been as an imbecile"; the distress of the mother was supposed to have caused the defective vision in III. 6. Of the mother's eleven siblings one, II. 9, died aged 70, very deaf, and nine died of phthisis; her mother, I. 8, also died of phthisis aged 47.

The father, II. 6, and his parents saw well, all his siblings saw well, but one of them, II. 1, died in a lunatic asylum.

Of the siblings of III. 6, III. 7 was "short-sighted"; III. 4, 9 and 11, with their children IV. 1 to 4, all had good vision. No consanguinity. Bibl. No. 301.

Fig. 164. *Usher's Case* 25. Two cases of retinitis pigmentosa in half-brothers, each of whom had a positive Wassermann. IV. 16, aged 24 (1901), had been night-blind since early childhood; his refraction was R. myopia 4 D., corrected V. = $\frac{6}{36}$, L. V. = finger counting at 1 metre; he had a left central corneal nebula and an anterior polar cataract; marked divergent strabismus; field of vision much contracted,

R. field to 10°; the discs were a pale yellowish colour with soft looking margins, retinal vessels much contracted; retinal pigmentation as delicate branched lines forming at places a network; vitreous opacities were present; he had convulsions in childhood, bronchitis at the age of 18 months, and had an irritable temper; Wassermann test positive. IV. 16 had had four children, of whom three had normal vision, one, V. 13, had high myopia at the age of 6 years, R. 10 D. in horizontal, 12 D. in vertical meridian, L. 8 D. in horizontal, 11 D. in vertical meridian, she had small myopic crescents. The three siblings of IV. 16 and their children, V. 12 to 20, saw well.

IV. 10, half-brother to IV. 16, aged 40 (1905), reported that he was "always short-sighted," and that his vision had gradually got worse; in 1905 he had perception of light, but in 1912 he had no perception of light in either eye; in 1905 he was seen to have typical retinitis pigmentosa and posterior cortical cataract: his left lens was opaque, and was dislocated into the anterior chamber; in 1912 there was diffuse total opacity of right lens; he was in good health and spirits, was an abstainer from alcohol and tobacco, and had no history of syphilis, but his Wassermann test was positive. His two siblings and the children of one of them saw well.

The mother of these two sibships, III. 5, had always been healthy, and had, at the age of 75, normal fundi. Her first husband, III. 1, died aged 60, from the result of a chill; he was reported to have held things near, but was not night-blind, and his sight did not get worse. Her second husband, III. 11, saw well.

No further defect of vision was known in the six grandparents, II. 1 to 6, in the great-grandparents, I. 1 and 2, or in any of their descendants, twenty-six of whom were examined by the author. No deafness and no insanity had occurred in any member of this pedigree. No consanguinity. Bibl. No. 301.

PLATE XVI. Fig. 165. *Usher's Case* 7. Four deaf-mutes, with retinitis pigmentosa, in a sibship of five; a paternal second cousin, IV. 20, was a deaf-mute; a paternal first cousin once removed, III. 13, was an imbecile; and one child of the normal sibling, V. 1, had a congenital digital deformity. IV. 11, aged 32 (1911), was a deaf-mute postman, with typical retinitis pigmentosa, his discs were pale, with several translucent, probably hyaline, bodies on them, the retinal arteries were markedly narrowed; retinal pigmentation was of the usual moss-like character and also pepper-like in some places; he had constant lateral nystagmus, and was night-blind; refraction hypermetropic; in 1900 R. V. = L. V. = $\frac{6}{36}$ partly, not improved by glasses, in 1911 R. V. = L. V. = $\frac{4}{60}$; fields much contracted; no history of illness; Wassermann test negative. IV. 10, aged 34 (1911), was mentally slow and a deaf-mute; he read type of about J. 2 at a few inches; he had typical retinitis pigmentosa; one large raised translucent body on right disc; posterior cortical cataracts; refraction hypermetropic; had constant lateral nystagmus and was night-blind; he did odd jobs. IV. 9, aged 36 (1911), was a deaf-mute saddler, with typical retinitis pigmentosa; R. V. = $\frac{6}{36}$ partly, hm. 2 D., L. V. = $\frac{6}{60}$, hm. 2 D.; he was night-blind, and fields of vision were contracted to about 10° in all directions, he had no nystagmus. IV. 6 was drowned in the river at the age of 27, he had been subject to epileptic fits for seven years previous to his death; he was night-blind and a deaf-mute; "his sight was a great drawback." In all these cases defect of vision was only noticed after they went to school, but deafness was noticed at a very early age. Their only normal sibling was a sister, who had normal vision; she had three children, of whom the eldest, aged 7, had a deformed left hand, the thumb and forefinger being complete, the other fingers terminating at the middle joint, all three had normal vision.

The mother, III. 28, had normal fundi, her parents and grandparents, with all their descendants, except the sibship IV. 6—11, had normal vision, and were free from congenital defects. I. 6, by her second husband, had children, II. 12, who all died of phthisis.

The father, III. 16, his two siblings, his parents and his grandparents, had good vision; one of his first cousins, III. 13, was an imbecile; one of his first cousins once removed, IV. 20, was a deaf-mute, with good vision. For further information concerning normal members of this pedigree see the author's original account. No consanguinity. Bibl. No. 301.

Fig. 166. *Usher's Case* 37. A single case of retinitis pigmentosa in a sibship of seven. III. 7, sailor, aged 48 (1897), reported a gradual failure of vision for 12 years; could never see so well as most people; in 1884 he one evening walked off a plank into the sea; denied venereal disease; R. and L. retinal pigmentation at periphery with moss-like arrangement, pigment was scanty; choroidal vessels exposed; no white atrophic choroidal patches; O. D. a dirty white colour, lamina cribrosa visible; retinal vessels contracted to mere threads; vitreous opacities; R. V. = p. l., L. V. = $\frac{3}{36}$; left field of vision contracted peripherally, most at upper part, where it was reduced to 22°; he died, some years previous to 1912, mentally defective and paralysed. His parents, II. 4 and II. 5, died old, and had good sight, as also had his four grandparents, none of whose descendants were known to have had defective sight except III. 7.

III. 7 married his first cousin once removed and had a daughter, V. 9, and three other children who died in infancy; by a second wife he had five living children, there had also been five miscarriages.

The mental defect in V. 5 and 7 was believed to be derived from their mother, IV. 3, who had a sister in a lunatic asylum.

The original pedigree is much more extensive than this reproduction, showing fourteen maternal cousins of III. 7, and nineteen paternal cousins, none of whom were known to have defective vision, also a large

number of more distant relations are included; one paternal first cousin, son of II. 1, also one more distant relation in generation V. were mentally defective. There had been a considerable amount of cousin marriage in the other branches of the family. The author examined 31 members of the pedigree. Consanguinity. Bibl. No. 301.

Fig. 167. *Usher's Case* 35. Two, possibly four, cases of retinitis pigmentosa, in a sibship of eleven. III. 12, aged 21 (1911), a hairdresser, had been short-sighted as long as he could remember, and had great difficulty in seeing at night; he was mentally slow, had some deafness, and had chorea when at school; he lost much blood over an operation on his ear at the age of 13; refraction, my. 3 D. in oblique, 4 D. in opposite meridian for each eye, corrected V. = $\frac{6}{12}$ in each eye; fields of vision contracted to within 20° except at outer part of field which extends to nearly 30°; discs were waxy, retinal vessels very narrow, choroidal vessels exposed, there was extensive moss-like pigmentation of the retina III. 13, aged 17 (1911), had marked night-blindness and deafness, which was complete in the right ear, the left ear heard a watch at one inch; he had no history of serious illness, but was not very strong; R. V. = L. V. = $\frac{6}{9}$, not improved by glasses; the discs were pale and waxy, the retinal vessels narrow, the choroidal vessels exposed, and much moss-like retinal pigmentation was present over the greater part of the fundus; his fields of vision were like those of his brother III. 12. III. 2 was reported by her mother to be affected in the same way as her brothers; she was obstinate and left home, and had not been seen for many years. III. 7 was reported to be deaf and night-blind; she had not been on speaking terms with her mother for sixteen years; she was married, but had no children. III. 3 died of croup, aged 2 years. III. 5 had chorea, and was very nervous; she was twice married, two of her three children by her first husband had died. III. 10 was seen and had normal fundi. III. 11 had rickets, and was not strong.

The mother of this sibship, III. 13, had normal fundi and was not deaf, but she was mentally peculiar and gloomy; her parents and her siblings, with their children, had good vision; one of her maternal aunts was paralysed at 15 and had fits.

The father, II. 6, had normal fundi; his parents and grandparents, with all their descendants, except the cases described above, had good vision and hearing.

Thirty-one normal first cousins, and other more distant relations, are described in the original extended pedigree. No consanguinity. Bibl. No. 301.

Fig. 168. *Usher's Case* 10. A single case of retinitis pigmentosa in a sibship of eight. III. 5, a female, aged 31 (1911), was unmarried; she had always been weak mentally and bodily, and had imperfect hearing; she had diarrhoea in infancy, "inflammation of lungs" at 16 months, never spoke until the age of 7; defective vision was first noticed at the age of 14 when she knocked against lamp-posts, it had gradually got worse; she had a violent temper, especially during menstruation, and once stabbed her mother in the arm, at other times she was morose. In 1903 she had posterior cortical cataracts, moss-like retinal pigmentation confined to a broad band at periphery of fundus, the extreme periphery was not pigmented; at the pigmented band the choroidal vessels were more exposed than elsewhere, and a few small bright white bodies were scattered here and there in the band region; O. D., a dirty white colour; retinal vessels very narrow; refraction, R. my. 1·25 D. in oblique meridian, 2·25 D. in opposite meridian; corrected V. = $\frac{6}{18}$ partly, L. my. as for R. with corrected V. = $\frac{6}{12}$ partly; fields of vision contracted. Eight years later (1911) pigmentation of retina was more marked, and night-blindness was severe, fields much contracted, speech defective, R. V. = L. V. = $\frac{6}{24}$ with correction; Wassermann negative. Her mother, II. 6, was healthy, with normal vision, but had a severe mental shock when $4\frac{1}{2}$ months pregnant with III. 5. Her father, II. 3, was excitable, but had a normal fundus; he had syphilis four years before his marriage. The grandparents had good vision.

Of the siblings of III. 5 the eldest, III. 2, had a normal fundus, and had one child, IV. 1, with normal fundus; III. 4, "quick tempered," had a normal fundus and one living child with normal fundus; III. 6—8 had good vision; III. 9 lived a few hours, said to have had club foot and a monster head; III. 10 had good vision.

A maternal uncle II. 4 died, aged 4, of "water in head."

The original and more extensive pedigree shows the eight great-grandparents of whom seven were reported to have normal vision, also nine first cousins and many more distant relatives are reported to have had normal vision. No consanguinity. Bibl. No. 301.

Fig. 169. *Usher's Case* 38. A single case of retinitis pigmentosa in a lazy, mentally feeble, illegitimate farm worker. IV. 17, aged 18 (1902), was night-blind, and had always been short-sighted; discs were a good colour, the retinal arteries distinctly contracted, choroidal vessels much exposed; there was much typical pigmentation at the periphery of the retina; fields of vision were contracted; no vitreous or lens opacities; nystagmus on lateral movement of eyes; refraction, myopia 3 D. in each, corrected V. = $\frac{6}{60}$ in each; with light reduced, so as to allow a normal eye $\frac{6}{12}$, he did not read $\frac{6}{60}$. Vision was reported by his doctor to be not markedly worse nine years later.

III. 5, believed to be the father of IV. 17, had normal fundi, his parents, grandparents, his siblings and their children, all had good vision; he was married, and had nine children, of whom IV. 6 died in

infancy, the others, who were all under 13 years of age, saw well. III. 12, the mother of IV. 17, died aged 44; two of her siblings died aged 16, and several brothers and sisters died in infancy; she was married and had four children, of whom one, IV. 18, died aged 15, of spinal disease, the others had normal fundi. Her parents, II. 6 and 7, and two paternal aunts, II. 4 and 5, had good vision. No consanguinity. Bibl. No. 301.

Fig. 170. *Usher's Case* 6. Retinitis pigmentosa in two members of a sibship of five, the offspring of first cousins. III. 3, aged 23 (1911), had marked night-blindness but saw well in the day time; his fields of vision were much contracted; retinal arteries were narrow, discs were pale and waxy, retinal pigmentation was very extensive, reaching to the papilla; refraction emmetropic. III. 5, a fisherman aged 19, had always had defective vision, he was night-blind and his vision was becoming worse; R. V. = $\frac{1}{60}$, L. V. = $\frac{4}{60}$; refraction low hypermetropia: discs were pale, retinal arteries much narrowed, choroidal vessels exposed, much moss-like retinal pigmentation was visible all over the periphery of the fundus; fields of vision were contracted, and each had a complete ring scotoma; Wassermann test negative. Of their siblings III. 1 died aged 13, III. 2 and 4 had good vision. Their mother, II. 7, was considered peculiar, she had a normal fundus, and had no miscarriages; of her siblings, II. 8 died aged 47, mentally defective, she did nothing for herself and never had good sight; II. 9 and the elder of II. 10 saw well; the younger of II. 10 had a bad temper and drank, his sight was defective and was getting worse, but he was found to have myopia and no retinitis pigmentosa. II. 11 was a fisherman with defective vision, which his doctor reports to be getting worse. The parents, grandparents and three great-grandparents of II. 7 were reported to see well; her mother, I. 3, was seen to have a normal fundus. The father of III. 1—5, first cousin of his wife, had a normal fundus but he had a cleft palate, his parents had normal vision; the parents of I. 1 saw well; II. 4 had eight siblings, of whom five died in infancy, the others and their children saw well. The original pedigree shows twenty-three first cousins and many more distant relatives free from any known defect. Consanguinity. Bibl. No. 301.

Fig. 171. *Usher's Case* 18. A single case of retinitis pigmentosa in a sibship of eight. III. 11, aged 53 (1911), a male factory worker, had difficulty in seeing in dim light and in seeing at either side of him; no defect was noticed until he was aged 45; the discs were pale; retinal vessels much contracted, profuse retinal pigmentation typical of retinitis pigmentosa, with two patches at outer part of left fundus suggestive of "choroiditis"; opacities at posterior part of lenses. R. V. = $\frac{6}{9}$, L. V. = $\frac{6}{18}$ partly; fields of vision concentrically contracted to 10°; Wassermann negative. Of the seven siblings of III. 11, three died young, and the others, with the children of two of them, saw well.

III. 11 had six children, of whom IV. 4 had high hm. astigmatism, fundi normal; IV. 6 had periodic internal strabismus, refraction R. and L. hm. 8 D. in vertical, 9 D. in horizontal meridian; fundus normal; IV. 7 died in infancy; the others had normal vision.

The father, II. 5, had good vision; the mother, II. 6, was short-sighted, screwed her eyes up, could see in old age, only had glasses for the last few years of her life, which ended at the age of 89. Three of the four grandparents were known to have seen well. No consanguinity. Bibl. No. 301.

PLATE XVII. Fig. 172. *Usher's Case* 22. An isolated case of retinitis pigmentosa commencing late in life. III. 18, female, seventh born in sibship of eight, aged 64 (1905); night-blindness first noticed about the age of 55; she was married and had 8 children, no miscarriages; severe bleeding at menopause confined her to bed. In a light allowing $\frac{6}{12}$ to normal eyes she could not see $\frac{6}{60}$; refraction R. and L. hm. 1 D., R. V. = L. V. = $\frac{6}{9}$ with correction; right field of vision nearly full; discs were pale, rather yellowish, lamina cribrosa much exposed; retinal arteries narrow; typical moss-like retinal pigment in each eye confined to an area extending from the disc downwards but not reaching the periphery of the fundus; choroidal vessels over the whole fundus were conspicuous; no vitreous opacities. Four years later there was very little change in the appearance of the fundus, but both fields were contracted and in the left was an absolute partial ring scotoma; four years later, again (1913), a complete absolute ring scotoma was present in both fields, and the retinal pigment had increased considerably; Wassermann test negative. Both parents lived to old age and had good sight. Two brothers of the patient had cataract, three brothers and two sisters had good sight. Of her children IV. 18 died aged 4; IV. 26 died aged 21; the other six, also their children, saw well. The patient's grandparents and aunts and uncles, also many more distant relatives, were reported to see well; no deformities, insanity, or consumption known in the stock. No consanguinity. Bibl. No. 301.

Fig. 173. *Usher's Case* 29. Retinitis pigmentosa in a brother and sister, the youngest members in a sibship of fourteen. III. 19, aged 45 (1898), was rather deaf, and had never seen well in a dim light; at this time R. V. = L. V. = $\frac{3}{240}$, extensive retinal pigmentation with pallor of discs and narrowed retinal vessels were noted. In 1910 her R. V. was reduced to hand-movements at 8 feet, L. V. to finger counting at 6 feet; there was a slight opacity of posterior part of lens in each; moss-like retinal pigmentation extended over practically the whole fundus. She had married twice, but had no children. III. 20, aged 40 (1895), was rather deaf, and had noticed night-blindness for three years only; for him R. V. = $\frac{6}{18}$, L. V. = $\frac{6}{24}$; extensive retinal pigmentation was present at the periphery of the fundi, the discs were pale,

the retinal vessels much contracted, vitreous clear, and his fields were contracted to about 15°. There appeared to be some difference of opinion as to whether the defects in III. 19 and 20 were the result of snowballing when they had measles or were due to slaps on the heads from their drunken father.

The mother, II. 6, was a "clever" woman, and had no night-blindness or deafness; she died aged 69. The father, II. 1, a postman, had good sight and hearing. Eleven aunts and uncles were free from defect in sight and hearing; also the four grandparents and four great-grandparents were believed to see and hear well.

III. 20 had five children, one of whom died in infancy, the others and the children of two of them saw and heard well.

Of the siblings of III. 19 and 20, III. 1 had phthisis, III. 11 died in infancy, the others were believed to be free from inherited defects; six of them had children, some of them grandchildren and great-grandchildren; one boy in generation V. had mental defect, one girl in generation IV. was epileptic. The original pedigree is much extended, and shows forty-eight or more first cousins and many more distant relatives, all believed to be free from defects of sight or hearing; one maternal first cousin was mentally defective. No consanguinity. Bibl. No. 301.

Fig. 174. *Alleman's Case.* (Taken from Loeb.) Retinitis pigmentosa in the descendants of a woman, I. 2, who was herself affected. Of the fifteen children of I. 2—II. 2, a male, had retinitis pigmentosa; II. 3, a female, was said to suffer from night-blindness; II. 5, a male, had retinitis pigmentosa; II. 7, a male, had night-blindness; four children had normal vision, and seven children died young, and nothing was known about the condition of their eyes. II. 2 had four children, one male and one female, with retinitis pigmentosa, one child with normal eyes, and one who was said to be blind. II. 3 had two children with retinitis pigmentosa and one with normal vision. II. 5 had one child with normal vision. II. 7 had one child with retinitis pigmentosa and one with normal vision. No further information is given. No consanguinity recorded. Bibl. No. 261.

Fig. 175. *Machek's Case.* Retinitis pigmentosa in five siblings, the offspring of consanguineous parents, two sisters were normal and had normal children. The five night-blind siblings first showed symptoms of the disease at the age of 10, the youngest, a boy, was completely blind at the age of 18, the others, all girls, were blind at the age of 20. They had nystagmus, and myopia of 5 to 9·5 D.; only in two cases were typical pigment deposits to be seen; some defect of colour vision had been demonstrated in three of the cases. Consanguinity. Bibl. No. 110.

Fig. 176. *Aubineau's Case.* Retinitis pigmentosa in three siblings, the offspring of parents who were first cousins and who themselves were the offspring of first cousins. The mother died aged 75, and the father aged 78; a paternal aunt could see still at the age of 81, and there were no ocular affections known amongst the relatives on either side.

In the sibship III. 1—4, III. 1 represents two sons, one of whom died of cholera aged 47; and the other died aged 53, both had perfect vision. III. 2, a son, had never been able to go about alone, and had been almost blind after sunset; he had nystagmus, convergent strabismus of the left eye, and at the time of examination his vision was reduced to perception of light; the discs were yellowish, only two or three thread-like retinal vessels could be seen; the retina was pale yellow, and typical pigmentary deposits were present over the whole fundus. He became tubercular and died; a *post-mortem* examination was made of the eye. III. 3, Rosalie C., aged 44, had been paralysed for 4 years and had had ocular difficulties since her birth, she was however able to go about alone in daylight up to the age of 20; she now had nystagmus, strabismus, vision reduced to perception of light, and fundi similar to those of III. 2. III. 4, Marie C., aged 42, a very intelligent woman, had always had bad sight, she had nystagmus and myopia of 3 D.; in good daylight she was able to recognise a hand; her fundi were similar to those of her brother and sister. Consanguinity. Bibl. No. 219.

Fig. 177. *Chaillous' Case.* Retinitis pigmentosa associated with deaf-mutism in an only child of unrelated parents. III. 1, a deaf-mute boy, was always debilitated, and was unable to walk until he was three years of age; his parents noticed trouble with his vision from his earliest youth, but the condition appeared to remain stationary; he was emmetropic; R. V. = L. V. = $\frac{5}{15}$; fields were contracted; media normal; and there was pigmentation of the retina which was more marked on the inner and outer sides than above or below. This distribution of the pigment was noted also in the other deaf-mute cases of this author. Of the parents the mother was normal, the father died aged 27, he suffered from articular rheumatism and complained of severe headaches; he was said to be very short-sighted and suffered from night-blindness. Of the grandparents, I. 1 died of paralysis in old age; I. 2 died of cerebral congestion; I. 3 died, aged 43, of pneumonia, and was alcoholic; I. 4 was living, and normal. No consanguinity. Bibl. No. 266.

Fig. 178. *van der Hoeve's Case.* Retinitis pigmentosa, deaf-mutism and albinism in a sibship of six. III. 1 suffered from night-blindness, fundus not described. III. 2 had a completely albinotic fundus. III. 3, a deaf-mute boy, examined at age of 10, had R. V. = L. V. = $\frac{1}{2}$; fields of vision concentrically contracted; the papilla was grayish yellow and atrophic; the retinal vessels were narrowed, and there was

scanty pigmentation of the retina typical of retinitis pigmentosa; there were also yellowish white round spots posterior to the retinal vessels which the author considered to be retinitis punctata albescens. III. 4, a girl, seen aged 4, was deaf-mute and night-blind; she had contraction of fields of vision, atrophic papilla, narrowed retinal vessels and retinal or retino-choroidal changes; the author describes her as a case of atypical retinitis pigmentosa. III. 5 had normal sight and hearing. III. 6, a deaf-mute girl, was seen in her first year to have a completely albinotic fundus; the papilla was of a grayish colour, and the retinal vessels were narrower than normal; several months after her first birthday a single grayish white patch was seen in her fundus. The parents of this sibship were healthy and normal, there was no syphilis and no history of eye or ear disease in the ancestry; the grandmothers were cousins. The father's twelve siblings were healthy though one sister, II. 4, was a dwarf and a brother had a boy, III. 7, who was deaf and an idiot, had a right internal strabismus, and who had some abnormal pigment flecks in the periphery of his retina. Consanguinity. Bibl. No. 291.

Fig. 179. *Chaillous' Case.* Retinitis pigmentosa associated with deaf-mutism in several members of a sibship, the offspring of first cousins. III. 1, aged 24, was deaf-mute and blind; in her early childhood she had had some vision but became completely blind at 10 to 12 years of age; she was extremely intelligent. III. 2, a male, was born prematurely, and died aged 29 days. III. 3, a female, died aged 3, she was not deaf but had very little vision, and was only able to see to go about alone. III. 4 was a normal female, aged 18. III. 5, a normal female, aged 16. III. 6, a deaf-mute, aged 13, had never seen clearly, but the condition of his eyes appeared to be stationary; R. V. = $\frac{5}{10}$, L. V. = $\frac{5}{15}$; visual fields were contracted; media normal; there was some pigmentation of the retina. III. 7, a female, died aged 3, of tuberculosis; she was neither deaf nor blind. III. 8, aged 8, was a deaf-mute and blind; she had retinitis pigmentosa with very little pigment. III. 9, a female, died aged 14 months, of convulsions; she was a blind deaf-mute, and suffered from osteomalacia. Of the parents the mother was normal, and the father with normal vision had some affection of his vertebral column. Of the grandparents I. 1 and I. 4 were normal. I. 2 died of heart disease, and I. 3 was alcoholic. Consanguinity. Bibl. No. 266.

Fig. 180. *Derigs' Case.* Retinitis pigmentosa and deafness in two cousins, whose fathers were brothers and whose mothers were aunt and niece. II. 1, Eduard Huland, aged 43, had R. V. = $\frac{20}{100}$, L. V. = $\frac{20}{50}$; fields of vision were contracted; a very diffuse pigmentation reached to the papilla, the retinal vessels were narrowed, and there was choroidal atrophy; he also had posterior polar cataracts; his eight siblings all saw well. The patient had noticed a diminution of vision since childhood, he was also deaf. II. 3, Otto Huland, aged 17, had normal central vision, and read J. 1; there was some contraction of his fields of vision, and there was a diffuse epithelial atrophy reaching to the papilla, in the periphery of the retina were streaks of pigment; the papilla was not discoloured; the retinal vessels were narrow; the patient was also deaf. Consanguinity. Bibl. No. 112.

Fig. 181. *Magnus's Case.* A mentally defective man had six children, of whom five were deaf-mutes and one had retinitis pigmentosa; the mother of this sibship from another marriage with a healthy man had healthy children. No consanguinity recorded. Bibl. No. 142.

Fig. 182. *Gonin's Case.* II. 4, the sixth born in a sibship of nine, aged 24, had suffered from night-blindness since the age of 7 or 8 years, his vision was reduced to finger counting at 3 or 4 metres, and the ophthalmoscopic appearances were typical of retinitis pigmentosa. One of his siblings, the fourth born, who died aged 35, had retinitis pigmentosa. No consanguinity. Bibl. No. 218.

Fig. 183. *Derigs and Bayer's Case.* Retinitis pigmentosa in the second and last born members of a sibship of eight. II. 2, Daniel Lindenberg, was first examined by Bayer at the age of 20 years when his vision was $\frac{1}{5}$, fields were concentrically contracted, typical pigmentation was confined to the equatorial region, and he showed diffuse atrophic changes in the choroid. Derigs examined him twelve years later, and found that his condition had progressed; the boundaries of his fields of vision now were L. horizontal, outer 5°, inner 30°, L. vertical above 7°, below 10° with similar defects in the R.; the pigmentary deposits were extending towards the papilla, and posterior polar cataracts had developed.

II. 6, Wilhelm Lindenberg, was examined by Derigs at the age of 20. R. V. = L. V. = $\frac{20}{100}$; boundaries of fields of vision were L. temporal 65°, nasal 45°, above 30, below 23°; R. temporal 50°, nasal 45°, above 27°, below 15°; typical pigmentation of the retina was present; he also had R. divergent strabismus. Both brothers were night-blind. Three other brothers and two sisters had normal vision, one sister was reported to be "short sighted." No consanguinity. Bibl. Nos. 75, 112.

Plate XVIII. Fig. 184. *Holloway's Case.* III. 4, aged 34, had retinitis pigmentosa, complicated by albuminuric retinitis. She had posterior polar cataract of the R. lens, opacities in the vitreous, an oval disc with blurred margins and greyish coloration; the retinal vessels were reduced in calibre; there was a slight greyish haze over the posterior pole of the eye with a typical stellate figure in the macula region; deposits typical of retinitis pigmentosa reached almost to the macula region; there was contraction of fields with small central scotomata; V. = $\frac{5}{10}$. The patient had been marasmic as a baby, and from $2\frac{1}{2}$ to 8 years had attacks of probably petit mal; she had scarlet fever at 6 and measles at 9 years, to which she

attributes the origin of her retinitis pigmentosa, for she was blind for three days at that time; later she had severe pneumonia.

The patient had one living brother, who suffered from retinitis pigmentosa; one brother died aged 21, of tape worm; one brother died aged 7, of pneumonia, and all her four sisters died in childhood of diphtheria, measles, pneumonia or scarlet fever. These six siblings were said to have had good vision. Of the patient's three children IV. 1, a boy, aged 14, and IV. 3, a girl, aged 6, had good vision; IV. 2, a girl, aged 12, wore glasses, and was said to have defective vision.

A maternal aunt was markedly near-sighted, and her son was said to have had very defective vision since childhood. A maternal great uncle also had very poor eyes from his childhood, and was supposed to be near-sighted; he had been in an asylum for 35 years as a result, it was said, of a blow on his head. The parents, II. 3 and 4, had good vision. No consanguinity. Bibl. No. 272.

Fig. 185. *Magnusson's Case.* Retinitis pigmentosa in dogs. This is the only pedigree found showing the inheritance of retinitis pigmentosa in animals; it is claimed to be the first well-authenticated case of retinitis pigmentosa in the dog. The cases occurred in a valuable breed of Gordon Setters, and was believed to have been introduced into the stock by an imported unaffected dog named Ranger I. 2. Mated with I. 1, Ranger had a son, II. 1; mated with I. 3, he had puppies, including II. 2 and 3. These three puppies were normal.

II. 1, mated with his half-sister II. 2, produced six puppies, of which three males had retinitis pigmentosa, one male and two females were normal. II. 2, mated with her brother II. 3, had a litter of puppies, of which only one was preserved. She, III. 7, named Lisa Odinsheim, had retinitis pigmentosa. Lisa was then mated with Ranger, her grandfather on both sides, and produced five puppies, of which one male and one female had retinitis pigmentosa, two males and one female were normal.

Night-blindness was first noticed in these dogs at the age of about six months; in one case the dog became completely blind in four years. Ophthalmoscopic examination showed thread-like opacities in the vitreous, discs grey, retinal vessels very small; pigment was present as a coarse network. *Post-mortem* examination showed a severe degree of retinitis pigmentosa affecting chiefly the outer layers of the retina, but in places there was complete atrophy of the whole retina; the choroid was atrophic, the chorio-capillaris was thin and the vessels scanty, the larger choroidal vessels were normal. The pigment epithelium showed irregularity and proliferation, but the amount of pigment deposited in the retina was slight relatively to the extensive atrophy. No evidences of inflammation were found, the whole picture was characteristic of a slowly progressive atrophy. Consanguinity. Bibl. No. 276.

Fig. 186. *Maude's Case.* (Sent to Nettleship.) Retinitis pigmentosa in three siblings, members of a stock showing other forms of degeneracy. I. 2 died in old age of epithelioma of the vulva, her mental condition was good, and she had five children who all appeared to have normal vision. No information is given of I. 1. II. 2 had a son, III. 2, aged about 47 (1908), who was half-witted, and who had six children, IV. 1—6. Of these children the eldest was a congenital imbecile; IV. 4 had fits in infancy.

II. 3 and her husband were both alcoholic and arthritic, II. 3 also had Graves' disease with at one time ophthalmoplegia; she had at least one son, III. 3, who also was alcoholic. III. 3 married his first cousin III. 4, who drank more than was good for her, and had ten children, three of whom had retinitis pigmentosa. III. 4 also had a miscarriage, IV. 8. IV. 7 was under observation from the age of 8 (1894) until the age of 22 (1908), he had retinitis pigmentosa with optic nerve atrophy and greatly contracted fields at the age of 10 but was able to earn his living up to the age of 20 years. IV. 9 was very rheumatic and hysterical. IV. 11, at the age of 11 (1908), had V. $= \frac{6}{24}$ in each eye, choroids markedly thin, discs pale, retinal arteries narrowed, some patches of pigment in the equatorial region. IV. 12, two years younger than IV. 11, had V. $= \frac{6}{36}$, and slight hypermetropia; the ophthalmoscopic changes were similar to those of her sister but rather less advanced. One of the brothers, IV. 10, was examined, and found to have a normal fundus. IV. 13 died aged 3 months, of general tuberculosis. IV. 14, aged 3 (1908), was not examined.

The mother of this sibship, III. 4, was the daughter of II. 7, and had three normal siblings. II. 8 had two normal children. II. 5 was married but had no children; she was extremely hysterical. Consanguinity. Bibl. No. 251, pp. 345—6.

Fig. 187. *Neuffer's Case.* (Taken from Nettleship.) Two healthy first cousins, have three deaf-mute sons who are blind from retinitis pigmentosa, and one normal daughter, who married and had a son, who had retinitis pigmentosa. Consanguinity. Bibl. Nos. 251, p. 29, 176.

Fig. 188. *Roy's Case.* Retinitis pigmentosa in three siblings, their father, and their paternal grandmother; only one case was examined. III. 1, aged 29, the editor of a paper, was reported to have had defective vision at the age of one year; he himself had noticed for a long time that his vision was dim, and he thought the condition was stationary; he was almost blind in the evening, and could only see straight in front at any time; he had no history of severe illness, and was not syphilitic; R. V. = L. V. $= \frac{20}{30}$; visual fields were contracted to the 10° circle for white and still more markedly for colours; the discs were hazy, and pigmentation of the retina was typical. Of his siblings five brothers and one sister

had normal vision, one brother who was dead, and his youngest sister aged 12, had retinitis pigmentosa. The parents were living, the mother, aged 56, was normal; the father, aged 70, suffered from severe headaches and was night-blind, he had spectacles at the age of 16, but they did not help his defective vision. The paternal grandmother was blind at the age of 60, and had suffered in her early years in the same way as her son II. 2. No consanguinity recorded. Bibl. No. 184.

Fig. 189. *Wilbrand and Saenger's Case.* II. 3, aged 40 years, had changes due to choroiditis in the region of the papilla, she also had pigmentary disturbances, which are not described in detail by the author, and myopia of 4 to 5 D.; R. V. = finger counting at $\frac{1}{2}$ m., L. V. = finger counting at $1\frac{1}{2}$ m.; she had bilateral incipient cataract. A younger brother saw badly, and was night-blind. Two children of an aunt were similarly affected, as also were the children of a sister. The patient had no children; she complained of headaches. The author considers that the choroidal changes and character of the fields of vision were such as to suggest a diagnosis of disseminated chorio-retinitis, whilst the pigment flecks and the family history of night-blindness suggest that the case should belong rather to the retinitis pigmentosa group. No consanguinity. Bibl. No. 264.

Fig. 190. *Darier's Case.* Retinitis pigmentosa in two brothers, their three sisters had normal vision. III. 1, a butcher, aged 31, complained that he had myopia; R. V. = $\frac{1}{40}$, L. V. = $\frac{1}{30}$; visual fields were contracted to $\frac{1}{3}$ the normal area; the papillae were pale and blurred, the retinal vessels were narrowed; the fundus showed very little pigment, but some typical moss-like deposits were present in the periphery; the papillae were surrounded by a narrow zone of choroidal atrophy; this patient was night-blind. III. 2, aged 18, also a butcher, had never had good sight and had been night-blind since infancy; R. V. = $\frac{1}{3}$, L. V. = $\frac{1}{2}$; the fields were reduced to give central vision only; the papillae were rosy and blurred, the retinal vessels very narrow; no pigmentation was visible in the retina.

The father, II. 1, had very good eyes, the mother was said to be myopic; the maternal grandfather became blind at the age of 30. No consanguinity. Bibl. No. 148.

Fig. 191. *Hutchinson's Case.* II. 2, aged 57 when examined, reported that he could see well until he was aged 18, when his sight began to fail, especially at night; at about the age of 37 it had failed more rapidly but the condition had now appeared to be stationary for about five years; he had had no pain in his eyes but complained of muscae occasionally; night-blindness was marked, vision was reduced to counting fingers; the discs were greyish white with blurred margins, the retinal vessels very narrow; around each disc was a greyish white area; at the periphery were very extensive accumulations of coal-black pigment beneath which the choroid was seen to be yellow and speckled with white. II. 2 had twelve children, all of whom were healthy but one; a daughter, aged 19, reported that "her sight left her at night and had been failing for about a year"; the ophthalmoscope showed an early stage of retinitis pigmentosa. No consanguinity. Bibl. No. 65.

Fig. 192. *Jeffries' Case.* II. 3, aged 19 years, had been more or less amblyopic since childhood and suffered from night-blindness; the condition had progressed and he carried on his work as shoemaker with difficulty; he had typical retinitis pigmentosa. The patient had three brothers and three sisters, his eldest brother, II. 1, aged 36, had such bad vision that he was unable to work; also a sister, aged 25, had very bad sight but she could see better than II. 1. The mother, I. 2, had died about nine years before, she had good eyes. The father, aged 60, also had good eyes. The patient had good general health and intelligence. No consanguinity. Bibl. No. 61.

Fig. 193. *McCreight's Case.* Retinitis pigmentosa in two siblings the offspring of "cousins." II. 1, aged 25, had had bad vision since she could remember but it had become noticeably worse the last two years; she could not read but was able to attend to her house duties; V. = finger counting at 8 feet; she had lateral nystagmus and anterior polar cataract in each lens; her visual fields were contracted to within 10° of fixation point; the ophthalmoscope showed typical changes in the fundus. Her brother, II. 2, also had typical retinitis pigmentosa. Consanguinity. Bibl. No. 190.

Fig. 194. *Darier's Case.* Retinitis pigmentosa in II. 1, aged 32, who had been night-blind since infancy; the condition was at an advanced stage and the fundus showed typical changes; R.V. = L.V. = $\frac{1}{4}$. Two siblings, aged 30 and 28 respectively, were night-blind, three siblings had normal vision. The father, aged 64 and the mother aged 60, had good health and very good vision. No consanguinity recorded. Bibl. No. 148.

Fig. 195. *Darier's Case.* Retinitis pigmentosa in a father and two of his six children. I. 1, aged 64, was almost blind with retinitis pigmentosa; his wife was not related to him and had good vision. II. 1 was night-blind but still had fair vision, her defect was first noticed at the age of 15 years. II. 2, aged 19, was night blind, her visual fields were greatly contracted, R.V. = $\frac{1}{2}$, L.V. = $\frac{1}{3}$, and her fundi were typical of retinitis pigmentosa. No consanguinity. Bibl. No. 148.

Fig. 196. *Derigs' Case.* Retinitis pigmentosa with atrophic changes in the choroid associated with ectopia lentis and corectopia in a brother and sister. II. 1, aged 27, had R.V. = finger counting at 5 feet or with + 4 D. = finger counting at 20 feet, L. V. = finger counting at 3 feet, with + 4 D. at 5 feet. II. 2, aged 21, had L. V. with + 4 D. = $\frac{5}{200}$, R. V. = perception of light only; ophthalmoscopic examination was made in each case. No further information is given. No consanguinity recorded. Bibl. No. 112.

Fig. 197. *Jeffries' Case.* II. 1, a farmer, aged 33, was well developed, healthy, and fairly intelligent, but he had never seen so well as other people; at the age of 21 he had "lung fever" and his vision was worse after this; he was now only able to see to count fingers, but could read up to three or four years ago; there was an abundant deposit of pigment reaching to the papilla; floating opacities were present in the vitreous and there was a delicate web-like deposit on the posterior capsule of both lenses. The patient had five sisters who all had good vision, his one brother, II. 2, aged 44, had gradually become nearly blind. A maternal uncle, I. 3, had also gradually lost his sight before the age of 45.

The mother, I. 2, aged 67, was reported to be "near-sighted." No consanguinity. Bibl. No. 61.

Fig. 198. *Ryerson's Case.* (Taken from Loeb.) Retinitis pigmentosa in four siblings, the offspring of first cousins. The parents were said to be without visual defects. No further information is given. Consanguinity. Bibl. No. 261.

Fig. 199. *Carpenter's Case.* Retinitis pigmentosa in three members of a sibship of five. II. 1 had noticed defective vision since she was aged 6; she was night-blind and had extensive pigmentation of the retina. Her brothers, aged 18 and 16, noticed impaired vision at the ages of 12 and 10 years respectively; they were not night-blind, the elder showed the usual pigment deposits in the retina, the younger had no pigmentation. The three siblings had ring scotomata and contracted visual fields. No history of syphilis. Two sons of the mother's brother were believed to be similarly affected but were not examined. No consanguinity. Bibl. No. 287.

Fig. 200. *H. Schmidt's Case.* I. 1, a peasant, aged 55, had seen badly with his right eye since childhood; it was found to be completely amaurotic except for a very small portion of the outer quadrant of the field of vision where he could still see fingers at a near distance; on ophthalmoscopic examination atrophy of the disc was found with some narrowing of the vessels; left eye was normal. I. 2 had normal eyes and there was no history of syphilis in either. Of their three children, II. 1, a girl, aged 27, had concomitant convergent strabismus, oscillatory nystagmus at times, was emmetropic, had good visual acuity and no night-blindness; the papillae were of a particularly dull grey colour flecked with small white spots on the outer side, the margins were blurred, the vessels unusually narrow; in other respects the fundi were normal. The second daughter, II. 2, aged 21 years, and also her brother, aged 17, had typical retinitis pigmentosa with pale discs, narrowed vessels, and scattered deposits of pigment in the retina; in both cases the condition was more advanced in the right eye than in the left; each had suffered from night-blindness and diminution of vision since childhood. II. 2 also had nystagmus and convergent strabismus. No consanguinity recorded. Bibl. No. 88.

Fig. 201. *Reinecke's Case.* II. 1, a patient suffering from retinitis pigmentosa, reported that two of his siblings suffered from night-blindness, and three siblings were hard of hearing. The parents were first cousins. No further information is given. Consanguinity. Bibl. No. 179.

Fig. 202. *Wilbrand and Saenger's Case.* Retinitis pigmentosa in three sisters. No further information given. No consanguinity. Bibl. No. 264.

Fig. 203. *Thompson's Case.* Superficial choroidal atrophy, without subjective symptoms in a woman, aged 57, whose father, and whose three nephews (brothers), probably suffered from atypical retinitis pigmentosa. II. 1, seen, aged 57 (1901), was found to have in each fundus an area of superficial choroidal atrophy with well-defined margin around the disc; beyond this area there was a good deal of pigmentary disturbance, the macula was comparatively normal; the changes were remarkably similar in each eye; R. V. $= \frac{6}{9}$ (3 letters), L. V. $= \frac{6}{6}$ (3 letters); fields of vision were very nearly full, no scotomata were present and the patient was not night-blind; her retinal vessels were not narrowed. She reported that her father who died 30 years before had always stumbled against things on account of his bad sight, and yet he could see to read a small print copy of the Bible; he did not go blind. Three of her nephews (brothers) suffered from night-blindness. III. 1 was seen to have minute visual fields with V. $= \frac{6}{9}$ in each. III. 2 had pigment changes at the macula; an irregular but well-defined area of normal choroid round the macula, with atrophy of the chorio-capillaris and pigmentary changes beyond this area; retinal vessels of a fairly good size; visual fields were full peripherally but ring scotomata were present; R. V. with $-2{\cdot}5$ D. $= \frac{6}{6}$, L. V. with $-3{\cdot}0$ D. $= \frac{6}{12}$. III. 3 was reported to be getting to see as badly as his grandfather, and to be afraid to go out after dark. The condition was progressing in the three brothers. The general health of the family was good. No consanguinity. Bibl. No. 216 *a*.

Fig. 204. *Bane's Case.* III. 1 was first examined in 1895 when she complained of having had poor vision with night-blindness since childhood; R. V. = L. V. $= \frac{6}{24}$, with correction $= \frac{6}{15}$; the discs were a dull muddy colour, the retinal vessels small, and typical retinitis pigmentosa was present; her fields were contracted to 15° from fixation point. In 1899 vision was reduced to $\frac{6}{30}$; in 1915 she complained of rapid failure of vision during the last six months, with pain and headaches, there was an increase of visible pigmentation and her vision was limited to the central part of the field. Her parents were unrelated and had nine children, of whom two daughters had retinitis pigmentosa. An aunt of her father, I. 3, and also a cousin on her father's side, were said to be similarly affected. No consanguinity. Bibl. No. 303.

Fig. 205. *Darier's Case.* Retinitis pigmentosa associated with polydactyly. III. 3, a boy, aged 12, had been noticed to be night-blind since the age of 5 or 6 years; he was very dark and his fundus was of a slaty grey colour, the macula almost black; his fields were reduced to central vision only; R. V. $= \frac{1}{3}$, L. V. $= \frac{1}{10}$; the retinal vessels were narrowed; there were no typical pigment deposits of the bone corpuscle type but black points of pigment could be seen here and there along the course of the vessels; he had six fingers on each hand and six toes on each foot. Two sisters older than the patient and one sister younger had good vision; two brothers had died, one aged 3 years, the other aged 7 months, each had twelve fingers and twelve toes. The parents were not night-blind; a maternal uncle had bad sight and coloboma iridis; the paternal grandfather had lost an eye (cause not given). No consanguinity. Bibl. No. 148.

Fig. 206. *Reinecke's Case.* Elsie M., aged 19, III. 1, her mother, II. 2, and all her siblings, also her maternal grandfather, I. 1, and two of her three siblings suffered from night-blindness. The author gives no further information, but since he quotes the case as an example of inherited retinitis pigmentosa we assume that the night-blindness was associated with this condition and was not of the congenital stationary type without fundus changes. No consanguinity recorded. Bibl. No. 179.

Fig. 207. *Drinkwater's Case.* Retinitis pigmentosa in the direct line of descent in three generations. I. 3, an affected female, had two brothers and four sisters, all of whom had normal vision; she married, and had two sons, II. 2 and 3, who both had retinitis pigmentosa. II. 2 married and had three children of whom two were sons with normal vision, one a daughter with retinitis pigmentosa. No further information given. No consanguinity recorded. (Unpublished, sent to K. Pearson.)

Fig. 208. *Volden's Case.* II. 1, aged 19, had for both eyes V. $= \frac{18}{20}$; his fields of vision were concentrically contracted, the R. to the 15° circle and the L. to 18°; he had no opacities of the lens and no pigmentation of the retina, but there was a fine white stippling of the choroid present in the equatorial zone; no mention is made of night-blindness. This is possibly a case of retinitis pigmentosa *sine pigmento.* The mother and six of the patient's seven siblings were said to suffer from a diminution of vision. The case is rather doubtful; it is included here since it has been quoted in the literature as a case of inherited retinitis pigmentosa. No consanguinity. Bibl. No. 94.

Fig. 209. *McCassy's Case.* Retinitis pigmentosa in three sisters, aged 15, 18, and 22, respectively; the eldest had noticed gradual diminution of vision for six or seven years. All were night-blind, there was no choroidal atrophy, opacities of the vitreous or involvement of the optic nerve. Parents were first cousins. Consanguinity. Bibl. No. 189.

Fig. 210. *Mooren's Case.* Four cases of retinitis pigmentosa in a sibship of eight. No consanguinity recorded. Bibl. No. 40.

Fig. 211. *Sambuc's Case.* Retinitis pigmentosa in six siblings, the only members of a sibship of fourteen who survived the age of 3 years; thus six males, the first, second, eighth, ninth, tenth and twelfth born, died under the age of 3, two twins, the last born, died aged a few months, the surviving two males, and all the four females, had retinitis pigmentosa. This account is taken from Nettleship who reports from a thesis published by the author in Bordeaux in 1896. The title of the thesis is not given, and we have been unsuccessful in our efforts to see it. No consanguinity recorded. Bibl. No. 251, p. 343.

PLATE XIX. Fig. 212. *Mücke's Case.* This is a very interesting pedigree showing retinitis pigmentosa in two or more sibships with night-blindness, high myopia, congenital deafness and other inheritable defects in several branches of the family. I. 1 and 2 were believed to have normal eyes; they had three children, II. 4, 6 and 7, who all had apparently normal vision and who married apparently normal individuals. II. 4 had a son, III. 4, who had high myopia. II. 6 had a son, III. 5, with normal vision. II. 7 had a daughter, III. 6, who is reported to have suffered from night-blindness.

III. 4 married III. 3 who was night-blind and they had two apparently normal daughters, IV. 4 and 6. The parents of III. 3 were normal, and her brother, III. 2, was normal, but the descendants of III. 2 were not free from eye defect. III. 2 married a healthy woman, III. 1, and they had a normal daughter, IV. 2, who married a healthy man, IV. 1, and had two daughters, of whom V. 1 had high myopia, V. 3 became completely blind after scarlet fever; V. 1 had a short-sighted daughter.

IV. 4 married twice; by her first husband she had a daughter, V. 4, who had always suffered from a recurrent inflammatory eye affection of an unknown character; by her second husband, IV. 5, she had two daughters, of whom V. 6 had high myopia and perhaps also, according to the statement of the priest, suffered from night-blindness; V. 8 had some eye affection "after catching a cold."

III. 5 married his first cousin, the night-blind III. 6; they had three normal sons, IV. 7, 8 and 9 who all transmitted eye disease and other hereditary defects to their descendants.

IV. 7 married his second cousin, IV. 6, the second normal daughter of III. 3 and 4; they had nine children of whom three died young, V. 11, 12 and 15 had retinitis pigmentosa, V. 13 had high myopia, V. 16 and 17 were normal. V. 11, female, aged 63 (1884), had typical retinitis pigmentosa, her fields of vision were much contracted on all sides and her vision was reduced to hand movements only. V. 12, unmarried, female, aged 53 (1877), saw badly as a child, especially at night; she had marked concentric contraction of fields; vision was reduced to hand movements; she had posterior polar opacities of both

lenses; her fundus showed a large number of white flecks in the central regions and pigmentary deposits in the periphery; the discs were atrophic and the retinal vessels very narrow. V. 15, unmarried, female, aged 51 (1877), had the same affection as V. 12, and her fundus showed the same condition at a less advanced stage; he was able to count fingers at $\frac{3}{4}$ m. V. 13 was the only member of this sibship who had children, she had a normal daughter, VI. 5, and a son, VI. 3, who was myopic and who had bilateral corneal opacities as a result of fascicular keratitis in his youth; VI. 3 had five children all of whom had normal vision, but one of them, VII. 3, had suffered from deafness since his birth.

IV. 8 married IV. 11, who was also probably from a tainted stock, for though her parents, III. 7 and 8, and her brother, IV. 12, had normal vision, the two sons of IV. 12 were night-blind; they had three children, V. 18, 19, 20. V. 18 suffered in his youth from very marked short-sight and night-blindness; at about the age of 40 years he became blind, and was known in the district where he lived as "blind Joseph." V. 19 had the same disease and became also completely blind. V. 20 was born blind.

IV. 9 married a woman whose history was unknown, they had a normal son, V. 21, and a daughter, V. 23, who had nystagmus. V. 21 married a healthy woman and had seven children of whom five died young of phthisis, and one, VI. 7, married and had three children, of whom one, VII. 6, died of phthisis. V. 23 married a healthy man and had four children, VI. 13, 14, 16, 18, none of whom showed any hereditary anomalies; all four married, VI. 13 had three children, of whom two died young of phthisis, VI. 14 had nine children, of whom seven were normal, two had some congenital deformity of the foot. VI. 16 had three children, one of whom was stillborn. VI. 18 had four children, of whom two died young of an unknown cause, VII. 24 had meningitis and became blind in his first year of life, VII. 25 had typical retinitis pigmentosa *sine pigmento*. Consanguinity. Bibl. No. 327.

Fig. 213. *Fisher's Case.* A single case of retinitis pigmentosa associated with deafness. This is a section only of a family history of which records had been accurately kept for many generations; Nettleship published for the first time in 1909 that part of it which showed the occurrences of retinitis pigmentosa and deafness from which this record is taken.

V. 6, aged 45, had well-marked retinitis pigmentosa and was moderately deaf. Of her six siblings, V. 5 died young of phthisis, V. 11 was deaf but had good sight, V. 4, 7, 9 and 13 were normal.

There was a vague history of bad sight in IV. 13, first cousin once removed of V. 6, and in her aunt, III. 12.

The parents of V. 6 were second cousins and the father, IV. 9, had been deaf since early life; there was also a history of deafness from early life in II. 8, IV. 12, V. 11 and 14, the deafness being severe in II. 8 and IV. 12, moderate in the other cases.

VI. 2 had attacks of mania, VI. 6 died in infancy from "some defect in the larynx" and VI. 7, the two children of a deaf father, also died in infancy. Consanguinity. Bibl. No. 263, p. CLIV.

Fig. 214. *Darier's Case.* Retinitis pigmentosa in three brothers of a sibship of five; the two eldest siblings and the parents had normal vision. II. 2, aged 77, a blacksmith, had been night-blind since infancy; he had senile cataract but his fundus could be seen to show changes typical of retinitis pigmentosa; he ceased to work at his forge at the age of 67 on account of his cataract. He had three children who all had normal vision, and two of whom had children with normal vision. II. 4 and 5 were also blacksmiths; they continued to work up to their deaths at the age of 77 and 46 years respectively, they were said to be night-blind but no statement was made as to an examination of the fundus in either case. No consanguinity. Bibl. No. 148.

Fig. 215. *Nettleship's Case.* Retinitis pigmentosa the onset of which appeared to be determined by an attack of scarlet fever in five siblings, two other siblings died of the scarlet fever (one case of which was associated with diphtheria) and three siblings had neither scarlet fever nor retinitis pigmentosa. III. 1 had scarlet fever at the age of 3 years, her sight failed in childhood after the fever, but the exact time of onset was uncertain. When aged 33 (1882), V. was less than $\frac{6}{60}$, fields were full, colour vision normal, sight best in a bright light; there was epithelial disturbance all over the central area, the retina was rather hazy at the periphery but showed no pigmentation; the discs were rather pale and hazy, the arteries too small. Thus she had an atypical retinitis pigmentosa and further she was a sleep walker, eccentric, suffered at times from delusions and was reported to have had Graves' disease at one time. III. 2 had scarlet fever at the age of 8 years and gave the disease to his five younger siblings; his sight began to fail just after the illness and became gradually worse but he was able to take a degree at Cambridge at the age of 22 years; when aged 54 (1904) he could only spell out very large letters with a hand lens and for many years had been unable to read ordinary print; he disliked bright light and was not night-blind; changes found on ophthalmoscopic examination were similar to those found in III. 1 but there were some small collections of pigment on the diseased central area and sclerosis of some choroidal arteries; mental condition was good.

III. 3, aged 30 (1882), had had a progressive failure of vision since the scarlet fever; vision was eccentric and about 16 J.; colour sense good; she also disliked a bright light; the central area in each eye showed a large surface with loss of epithelium and slight pigment collections; the arteries were doubtfully shrunken, the discs pale and hazy. In 1904 she was reported to be almost the same and to have three grown up children with perfect sight.

III. 5 reported that her sight became bad very soon after the fever, at the age of 28 she could still see well enough to be a governess, and she was not blind at the age of 43 (1897), when she died of heart disease and dropsy; latterly her mind had failed; there was no record of an examination of her eyes.

The two next youngest were girls who died from scarlet fever, aged 4 and 3 years respectively, the younger of the two had also diphtheria.

III. 7, when aged 10 months, was ill at the same time as her siblings "either with scarlet fever or measles," and afterwards had "abscess in the ear"; as a child she could see to read fairly well, began + glasses at the age of 14: ten years later she had well-marked nystagmus, sight worse in a bright light, loss of nasal third of each field; she had very typical advanced retinitis pigmentosa and was reported to be nearly blind at the age of 36; she was emotional.

III. 8, 9 and 10 were born after the scarlet fever outbreak and never had the disease, the mental power of III. 8 and 10 was above the average, their sister, III. 9, was extremely hysterical and had more than once been out of her mind; her eyes were normal and all the three had perfect vision at the age of 40—44.

The parents were healthy and unrelated; the mother was the offspring of "distant" cousins. Consanguinity. Bibl. No. 251, pp. 159—61.

Fig. 216. *Reinecke's Case.* Mathilde H., aged 55, II. 2, had always been night-blind; her brother, her mother, and her son were similarly affected. No further information is given. The author quotes this as a case of inherited retinitis pigmentosa; we assume, therefore, that the night-blindness was associated with this condition, and was not of the congenital stationary type without fundus changes. No consanguinity recorded. Bibl. No. 179.

Fig. 217. *Nolte's Case.* This case was placed by Nettleship amongst his reported cases of retinitis pigmentosa *sine pigmento*; three members in a sibship of eight were affected, also their two first cousins in a sibship of four, two maternal great-uncles were reported to have been blind at school age. The condition was associated with epilepsy in three cases, and in one case only was night-blindness noted.

III. 6, aged 21, was of a robust build and well nourished; he looked stupid, stammered, and was mentally very feeble; he had typical epileptic seizures; on ophthalmoscopic examination there was found to be atrophy of the optic nerve, marked narrowing of the retinal arteries, the retina was of a greyish colour, and the pigment epithelium was atrophied, producing a fine granular appearance in the fundus; he had small bilateral anterior polar cataracts. His father reported that diminution of vision was first noticed after a severe illness with brain symptoms and diarrhoea, which kept him in bed for six or seven weeks at the age of three; the condition had progressed from that time. An examination of his eyes in 1886, when he was aged 12, was reported.

III. 7 was healthy until the age of 4, when she developed epilepsy, and a diminution of vision was noticed which progressed to almost complete blindness; no ophthalmoscopic examination was reported. At the age of 14 she was sent to a hospital for epilepsy, and died later in epileptic coma.

III. 10, aged 8 (1904), was healthy, but of rather slow, dull intelligence; he could read and write at the age of six, when first a gradually progressive diminution of vision was noticed; at the age of 14 he was able to count fingers only; the ophthalmoscopic appearances were similar to those of his brother III. 6.

These siblings had four normal sisters aged 27, 24, 15 and 13 respectively, and one normal brother, aged 18.

The father's sister, II. 2, had four children, of whom two sons, aged 19 and 12 years respectively, were normal, one daughter, who died aged 19, had become blind, and a daughter, aged 18, had seen badly since her ninth year and was night-blind, she also had epileptic seizures. No consanguinity. Bibl. No. 191.

Fig. 218. *Neuffer's Case.* (Taken from Nettleship.) Five cases of retinitis pigmentosa in three sibships in a pedigree showing freedom from the disease in the direct line of ancestry for four preceding generations in the case of two sibships, V. 1 and 2 and V. 3 and 4, and for three preceding generations in the third case IV. 1.

V. 1 and 2 were first cousins to V. 3 and 4. IV. 1 was second cousin once removed to the other affected members. Nothing was known of II. 1 and II. 4. No consanguinity recorded. Bibl. Nos. 251, p. 22, 176.

Fig. 219. *Frickenhaus' Case.* (Taken from Nettleship.) Retinitis pigmentosa in a brother and sister, the offspring of healthy first cousins; they have one healthy sister IV. 2, who is married, and has three normal children. Consanguinity. Bibl. Nos. 251, p. 41, 81.

Fig. 220. *E. Schmidt's Case.* II. 1, aged 38, with V. $= \frac{1}{40}$ in each and fields irregularly contracted was seen to have diffuse choroidal atrophy, atrophy of the papilla and narrowed vessels; her father, two siblings, and the child of a normal sister, were said to be night-blind. No further information is given. The author includes the above in his series of observed cases of retinitis pigmentosa. No consanguinity recorded. Bibl. No. 163.

Fig. 221. *Böhm's Case.* Two brothers married two sisters respectively, their cousins. One marriage resulted in two children, of whom the elder, a boy, was epileptic but had normal vision, his brother had retinitis pigmentosa. The other marriage resulted in four children, of whom the eldest, a boy, became blind at the age of 40 from retinitis pigmentosa; his younger brother and two sisters had normal vision. Consanguinity. Bibl. No. 317.

PLATE XX. Fig. 222. *Abelsdorff's Case.* Retinitis pigmentosa in probably four generations. The patient III. 2, aged 24, and her sister, aged 19, presented a typical picture of retinitis pigmentosa; a brother was reported to have good sight. The patient's mother and her grandmother were night-blind from early childhood, the grandmother became blind at the age of 56, the mother was blind at the age of 44. III. 2 had three children, a boy with normal vision, a daughter, aged 6 months, who could not be examined, and a daughter, aged 4 years, was already showing changes in the pigment epithelium in the form of numerous white spots in the periphery of her fundi. No consanguinity recorded. Bibl. No. 229.

Fig. 223. *Ewing's Case.* (Published by Loeb.) Retinitis pigmentosa in four successive generations. I. 1 suffered from night-blindness; her son, II. 2, had well-developed cataract in the right eye, the left eye was aphakic and retinitis pigmentosa was present. Of the children of II. 2, a son III. 2 had marked cupping and pallor of the right disc with retinitis pigmentosa in the peripheral portions of both eyes; a son, III. 3, was troubled a little with night-blindness and some small pigment spots were present in the fundus, vessels were of normal size; three years later the night-blindness had increased, vision was normal in both eyes and characteristic stellate pigmentation was present. III. 4, daughter of II. 2, had always suffered from night-blindness; ophthalmoscopic examination showed one fundus to be normal in every respect, in the other eye a small black spot was present in the upper peripheral portion of the fundus, in the lower portion there was a slight greyish retinal change.

IV. 1, daughter of III. 2, had been night-blind since early childhood; R. V. = L. V. = $\frac{2}{15}$; fields normal; no pigmentation of the retina; three years later there was typical pigmentation of both retinae with moderate contraction of fields. No consanguinity recorded. Bibl. No. 261.

Fig. 224. *Nettleship's Case.* A single case of retinitis pigmentosa in a girl, the offspring of first cousins; her only sibling died of measles aged 2 years. There was no information of the father's family; the mother's family was believed to be free from the disease. Consanguinity. Bibl. No. 251, p. 41.

Fig. 225. *Nettleship's Case.* Retinitis pigmentosa in a brother and sister, II. 2 and 4, who were the offspring of healthy first cousins. It was reported that they both went blind at about the age of 45 of "optic nerve decay"; they each lived to an advanced age. II. 2 married twice and had normal children by each wife; a daughter by the second marriage, III. 4, was examined by the author; a son by the first marriage, III. 2, married his first cousin and had four children, of whom the eldest, a girl, had contracted fields of vision and suffered from night-blindness. Consanguinity. Bibl. No. 251, p. 29.

Fig. 226. *Kaupp's Case.* Retinitis pigmentosa in two brothers; the mother, the maternal grandmother and other relatives were reported not to have seen well. III. 1, aged 50, had had near vision as a child and had never learned to read or write; he was addicted to drink; for 8 years he had noticed a gradual diminution in his sight, especially in the evening; he was examined and found to have typical retinitis pigmentosa with greatly contracted fields, narrowed retinal vessels, whitish papilla, and pigmentation at the periphery of the fundus; he was treated with strychnine with an improvement. The author describes the appearance of his fundi at three examinations covering a period of years. III. 3, aged 49, had suffered from night-blindness as a child but had seen well in the day until two years before the examination, since then there had been a rapid diminution of vision; his fundus was typical of retinitis pigmentosa but in addition there were some greyish white flecks described in the choroid. V. R. = $\frac{1}{6}$, V. L. = $\frac{1}{20}$; fields showed concentric contraction. The two sisters of III. 1 and 3, and the three children of III. 3 had good sight. No consanguinity. Bibl. No. 162.

Fig. 227. *Nettleship's Case.* Retinitis pigmentosa in a father and one of his six children. II. 5 had no noticeable night-blindness until the age of about 32 when his fields of vision were full and V. = $\frac{5}{5}$, but the retinal arteries were slightly narrowed and the discs were palish and blurred; no pigment changes could be found; two years later the arteries were smaller and V. = $\frac{5}{12}$, the pigment epithelium was stippled and the choroidal vessels sclerosed but there was still no visible pigmentation of the retina. His father, I. 1, died aged 57, of enteric fever, he had suffered from night-blindness for many years but could see fairly well by day up to the time of his death. His mother, I. 2, suffered badly from "dead fingers." One of the patient's sisters suffered from very severe chilblains. No defective vision or other degeneracies were known in other members of the family. No consanguinity. Bibl. No. 251, p. 347.

Fig. 228. *Cabannes' Case.* An atypical case of retinitis pigmentosa associated with other defects of vision. II. 1, Charles N., aged 28, had excellent vision up to the age of 12 when he first noticed a diminution in vision; this progressed, he was unable to read or write after the age of 16 and was unable to recognise people after the age of 25; he was unable to go about alone at night; he was found to have nystagmus, horizontal and rotary, and had central scotomata; his pupils reacted sluggishly; tension was normal; the retinal veins were a little increased in volume, the arteries were scarcely appreciable; the choroid appeared to be a little congested and there were multiple pigmentary deposits at the periphery; the macula region was normal; he complained of frontal headaches and had myopia of 3—4 D.

II. 2, aged 21, had myopia of 8 D.; he complained of headaches and a diminution of vision which began at the age of 13—15; V. = $\frac{1}{6}$ in 1903 and V. = $\frac{1}{10}$ in 1906; pupils reacted briskly; he was not night-blind; the retinal vessels were diminished, the veins perhaps a little tortuous; the papilla was pale and

showed some neuro-papillitis with slight atrophy; there was no peripheral pigmentation and no history of syphilis or alcoholism.

II. 3, aged 18, was emmetropic in the right eye with V. = $\frac{1}{6}$, he was myopic, 3—4 D. in the left eye with V. = $\frac{1}{10}$; he had noticed a diminution of vision from the age of 5—6 years; no scotomata were present and no night-blindness; the papillae were pale and vessels rather narrower than normal. The author suggested that II. 1 was a case of retinitis pigmentosa, II. 2 and 3 approached nearer to hereditary optic neuritis. No consanguinity recorded. Bibl. No. 240.

Fig. 229. *Wilbrand and Saenger's Case.* Retinitis pigmentosa in four siblings. II. 1, a girl aged 13, had typical retinitis pigmentosa, she had further some defects of the central nervous system shown by exaggerated reflexes and a marked lowering of sensibility to pain. II. 2, a boy aged 12, had typical retinitis pigmentosa. II. 3, a boy aged 10, had typical retinitis pigmentosa. II. 4, a girl aged 7, had typical retinitis pigmentosa and further she had exaggerated reflexes and reduced sensibility to pain in parts of her body. No consanguinity recorded. Bibl. No. 264.

Fig. 230. *Trousseau's Case.* Retinitis pigmentosa in II. 1, the child of first cousins. The father, I. 3, had retinitis pigmentosa and his brother, I. 2, was completely blind. The mother, I. 4, had amblyopia and strabismus of the left eye. Consanguinity. Bibl. No. 171.

Fig. 231. *Ayres' Case.* Third, fourth and fifth children with defective sight in a sibship of eight; only one case examined. II. 2, female aged 26, had noticed a gradual impairment of vision for some years, she was now unable to see to get about and was found to have very contracted fields and marked retinitis pigmentosa, the pigment extending beyond the equator of the eye. The parents were cousins, the mother had good eyes but the father's sight was very defective. Consanguinity. Bibl. No. 138.

Fig. 232. *Magnus's Case.* The three eldest members in a sibship of four became completely blind from retinitis pigmentosa at about the age of 8 years; the youngest, a boy aged 16, suffered from very defective vision but was not completely blind. No information is given of the parents. No consanguinity recorded. Bibl. No. 142.

Fig. 233. *Kerschbaumer's Case.* Retinitis pigmentosa in a blind peasant, I. 3, his sister, I. 2, and his daughter, II. 1. I. 3 had numerous other siblings and children who had normal vision. No consanguinity recorded. Bibl. No. 141.

Fig. 234. *Pufahl's Case.* Retinitis pigmentosa in two members of a sibship of four, the offspring of parents who were uncle and niece. II. 2, seen, aged 30, was night-blind and suffered from retinitis pigmentosa and deafness; he had seen badly for several years. His sister, II. 1, had died at the age of 34, she also had been night-blind and was affected in the same way as her brother; the disease had appeared in both cases in the same year of life. Consanguinity. Bibl. No. 95.

Fig. 235. *Derigs and E. Schmidt's Case.* Atypical retinitis pigmentosa with very marked atrophic changes in the choroid in two brothers. II. 1 was examined by Derigs when aged 16; R. V. = L. V. = $\frac{20}{20}$ with − 0·3 D.; fields were much contracted and very marked atrophic changes were present in the choroid and in the epithelial layer of the retina, in the macular region were brownish red pigment flecks; there was only a trace of pigment in the periphery typical of retinitis pigmentosa; the patient was rather backward in his development but no defects were found in other organs; the diminution of vision was first noticed after scarlet fever at the age of 6. His brother, II. 2, was examined some years later by Schmidt at the age of 14 when R. V. = $\frac{20}{30}$, L. V. = $\frac{20}{200}$, and he was diagnosed as chorio-retinitis pigmentosa with scanty pigmentation of the periphery of the retina. Parents were healthy, and six siblings had normal eyes. No consanguinity. Bibl. Nos. 112, 163.

Fig. 236. *Derigs' Case.* Unilateral retinitis pigmentosa in a woman aged 46. II. 1, Frau Merz, had R. V. = $\frac{110}{1000}$, field of vision for R. markedly contracted; she had a posterior polar cataract, a marked atrophy of the papilla and a profuse pigmentation of the equatorial zone; her diminution of vision had progressed since her youth. Her brother is described as having the same disease but it is not stated whether in his case the trouble is unilateral or bilateral. No consanguinity. Bibl. No. 112.

Fig. 237. *Grossmann's Case.* Retinitis pigmentosa in II. 2 who had seen badly since the age of 15, he was night-blind but was able to carry on his work in the day, V. = $\frac{6}{36}$; he also had six toes on each foot and six fingers on the right hand, left hand normal. A brother aged 20 had six fingers on each hand and six toes on each foot, he also had bad sight; the parents and other siblings were normal. No consanguinity. Bibl. No. 248.

Fig. 238. *Laycock's Case.* II. 1, a healthy girl aged 17, had had difficulty in distinguishing objects as soon as twilight came on since the age of 12; she could see perfectly well during the day; she had been somewhat deaf in childhood but this had gradually improved. II. 2, a boy aged 15, also suffered from night-blindness and rather defective hearing. II. 3, aged 13, a nervous and delicate looking boy, suffered from night-blindness and was much more seriously deaf than his elder siblings; throat was normal and beyond a free excretion of cerumen there was no discernible defect in the ears. II. 4, aged 10, was extremely deaf and had suffered from night-blindness for several years. II. 5, aged 7, was also extremely

deaf and had suffered from night-blindness for two or three years. The other five siblings had normal sight and hearing. It is unfortunate that no ophthalmoscopic examination was made in these cases. The history is only tentatively included in this section. No consanguinity recorded. Bibl. No. 56.

Fig. 239. *Wilbrand and Saenger's Case.* Of three children of blood-related parents II. 1, a son, had typical retinitis pigmentosa; II. 2, a daughter, had night-blindness with concentric contraction of fields, atrophy of the papilla, very narrow retinal vessels and white flecks in the periphery of the retina, no pigmentary deposits were to be seen. Another son, II. 3, was deaf. It is not stated whether there were any normal members of the family. Consanguinity. Bibl. No. 264.

Fig. 240. *La Gleyze's Case.* (Published by Nettleship.) Retinitis pigmentosa in the daughter of healthy first cousins and also in her first cousin. Consanguinity. Bibl. No. 251, p. 28.

Fig. 241. *Rodsewitsch's Case.* This case is of interest as being an illustration of retinitis pigmentosa *sine pigmento* seen at an advanced stage with no development of pigment having taken place. II. 1 had been night-blind since childhood; R. V. $= \frac{5}{200}$, L. V. $= \frac{2}{200}$; fields were contracted to fixation point; the papillae were pale, the vessels greatly narrowed, and nowhere were there any deposits of pigment to be seen. His mother was completely blind, and a brother and sister had weak sight. No consanguinity recorded. Bibl. No. 206.

Fig. 242. *Derigs' Case.* Retinitis pigmentosa in four siblings. II. 1, aged 36, Auguste Schmidt, had R. V. = L. V. $= \frac{20}{70}$, she had considerable contraction of her fields of vision, also posterior polar cataracts; the pigmentation was very marked and extended to the region of the papilla. II. 2, aged 32, had myopia of $\frac{1}{30}$ in the R. and hypermetropic astigmatism in the L. eye; his fields of vision were contracted but not very markedly, above and below to 30°, inner and outer to 40°; no ophthalmoscopic changes were present but he complained of night-blindness and was possibly a case of retinitis pigmentosa *sine pigmento*; he was reported to have a brother with the same difficulties. II. 3, Maria Schmidt, aged 24, had R. V. = L. V. $= \frac{20}{40}$; her fields were contracted R. above to 35°, below to 30°, temporal to 50°, nasal to 25° with similar changes in the L.; the pigmentation was less markedly developed than in her sister II. 1; she had posterior polar cataracts. Consanguinity. Bibl. No. 112.

Fig. 243. *Carruthers' Case.* III. 2, aged 19, reported that he had been night-blind since early childhood; his fields of vision were slightly contracted, R. V. = L. V. $= \frac{6}{12}$; no ring scotoma was present; the left fundus showed very little abnormality except retinal atrophy; in the right fundus the surface of the disc was raised about 1·5 D. above the adjacent retina, the macular region was oedematous and glistening striae could be seen especially marked between the macula and the disc; there was retinal atrophy and in one spot towards the nasal side of the fundus three or four faint but definite pigmented corpuscular figures were seen in proximity to the vessels. Urine was free from sugar and albumen; blood pressure 140; Wassermann test negative. The case was discussed and was decided to be retinitis pigmentosa with some acute process overlying the atrophic process; one observer noted fine floating opacities in the vitreous. The patient's sister, aged 24, and his brother, aged 17, also suffered from night-blindness and, from the description given by III. 2, appeared to suffer from ordinary retinitis pigmentosa. The parents and grandparents were normal. No consanguinity. Bibl. No. 308.

Fig. 244. *Ayres' Case.* III. 1, a carriage painter, aged 54 years, had suffered from night-blindness for 20 years; his fields were much contracted and pigmentation of the retina was well marked; he had an attack of acute glaucoma in the right eye and when seen the pupil was moderately dilated, T. = + 2 and R. V. = perception of light only; L. V. $= \frac{6}{64}$. III. 2, aged 47, also had retinitis pigmentosa, the pigment being sparsely scattered over the retina; she had no limitation of fields; R. V. $= \frac{15}{30}$, L. V. $= \frac{15}{25}$. III. 3 had defective eyes from an unknown cause. The maternal grandmother, I. 2, was night-blind. No consanguinity recorded. Bibl. No. 138.

Fig. 245. *Bellarminoff's Case.* Retinitis pigmentosa and glaucoma in a peasant, Iwan Nikiforoff, aged 40. III. 1 complained of pain in both eyes with marked diminution of vision; he began to see badly with the right eye a year previously and his left eye had been failing for about six months; earlier he had suffered from night-blindness and had seen coloured rings round the lamp; he had seen well and had not night-blindness in his youth. He was found to have R. T. = + 2, L. T. = + 1, marked dilatation of the anterior ciliary veins, anterior chambers small; pupils showed a medium dilatation, greater on the right side, with a sluggish reaction; the vision of the right eye was reduced to perception of light and for the left eye was greatly diminished, V. $= \frac{20}{40}$, and the field also was greatly contracted; media were clear except for a small opacity of the L. lens; the papilla showed a deep glaucomatous excavation, and towards the periphery of the fundus were seen typical deposits of retinitis pigmentosa.

The sister of the patient died aged 55 completely blind, also a maternal cousin was blind, no further details are given of these relatives. The father, II. 2, died aged 80 with his sight, and the mother could see at the time of her death when she was aged 70; she had suffered from night-blindness during pregnancy. The grandparents died with full vision. No consanguinity. Bibl. No. 172.

Fig. 246. *Blessig's Case.* Three cases of retinitis pigmentosa and two cases of glaucoma simplex in a

sibship of nine. III. 1, Sophie P., at the age of 62 had R. glaucoma simplex for which iridectomy was performed, at the age of 77 she had L. glaucoma simplex for which again iridectomy was performed. III. 2, Carl, was seen at the age of 48 to have retinitis pigmentosa with posterior cortical cataracts, papillae pale, R. V. $= \frac{2}{5} - \frac{2}{5}$, L. V. $= \frac{2}{10} - \frac{2}{5}$, fields contracted almost to fixation point; he had been night-blind since childhood and was deaf; he was seen at subsequent intervals and became almost blind; he was married and had normal children. III. 4, Emma, had normal vision and had normal children. III. 6, Julie, and her children had healthy eyes. III. 8, Emilie, was deaf, she had bilateral glaucoma simplex and was unmarried. III. 9, Robert, was night-blind from his youth and deaf; he was seen, aged 53, with typical retinitis pigmentosa, his fields were contracted to fixation point and anterior polar cataracts were noted; he married and had normal children. Fanny, III. 11, and Bernhart, III. 12, were unmarried and normal. Anna, III. 13, was night-blind and deaf; she was seen at the age of 46 to have advanced retinitis pigmentosa with her visual fields contracted to fixation point; she was unmarried. The parents, II. 2 and 3, were normal and unrelated. The paternal grandfather, I. 1, was blind in his old age. No consanguinity. Bibl. No. 214.

Fig. 247. *Bradburne's Case.* Five cases of retinitis pigmentosa in a sibship of nine, associated with glaucoma in three of the cases. I. 1 died aged 50; I. 2 died aged 80 with good sight. Of their eight children, seven saw well and one, II. 3, had been night-blind since her childhood, the condition following a severe attack of scarlet fever; she died aged 69, the mother of III. 1—9. III. 1 died aged 60 with good sight. III. 2 died aged 4 years from diphtheria. III. 3, aged 61, twin to III. 2, had well-marked retinitis pigmentosa, her sight had been very defective for the last twenty years; the cornea was quite clear and had a diameter of 11 mm.; anterior chamber was shallow; there was a small opacity in the centre of the lens; details of the fundus could not be seen owing to a slow nystagmus; T. was sub-normal; no vitreous opacities were seen; she had a history of severe attacks of pain in the left eye.

III. 4, aged 58, had well-marked retinitis pigmentosa; V. in each eye = finger counting at 3 m.; corneal diameter 12 mm.; anterior chamber shallow; T. sub-normal; there was marked degeneration of vitreous in which were large freely floating opacities; the R. lens showed a posterior capsular opacity; she had never had prodromata of glaucoma.

III. 5, aged 54, had no retinal changes and no prodromata of glaucoma; corneal diameter 12 mm.; anterior chamber shallow; pupils partially dilated; there was a considerable haze in the lens and some opacity at its centre; T. slightly sub-normal; no evidence of opacities in the vitreous; the R. disc had a deep physiological cupping equal to − 2 D. with steep sides, the L. disc had a deep funnel-shaped excavation equal to − 2·5 D.

III. 6 died aged 3. III. 7, aged 51, had had defective vision for a long time which was becoming worse; she had had attacks of pain five weeks previously in both eyes; corneal diameter 12 mm.; posterior polar opacities with general haze of lens obscured the details of the fundus; T. = + 1; pupils nearly fully dilated. Operation was performed for glaucoma.

III. 8, aged 50, had well-marked retinitis pigmentosa; she also had acute glaucoma in the L. eye and was entirely blind in the R. eye as a result of a similar attack some years earlier. III. 9 had well-marked retinitis pigmentosa; corneal diameter 11·5 mm.; anterior chamber shallow; media clear; R. V. $= \frac{3}{60}$, L. V. = hand movements; T. high. She had an attack of severe pain in the L. eye and operation for glaucoma was performed. No consanguinity was recorded. Bibl. No. 307.

Fig. 248. *Wider's Case.* Retinitis pigmentosa in six siblings with normal parents. II. 1 seen, aged 53, had suffered since his youth, his vision was reduced to hand movements and his fields were very small, he was hypermetropic and his fundi showed typical changes. II. 3, aged 48, had symptoms of retinitis pigmentosa since his youth and also had absolute glaucoma. There were four other siblings, all of whom were said to have retinitis pigmentosa, two of them being completely blind. II. 3 had five children with normal vision. No consanguinity recorded. Bibl. No. 137.

Fig. 249. *Heinersdorff's Case.* Retinitis pigmentosa associated with glaucoma. II. 1, aged 22, had suffered since his earliest youth from night-blindness and "short sight"; four or five months before examination he noticed cloudiness of his vision occasionally, and this condition had been constant for about a month; he also saw rainbows, and had pain in his eyes and headache. Three years previously he had been given spectacles—3·0 D. sph. He now had bilateral myopia of 6 D. and with correction R. V. = 0·45, L. V. = excentric hand movements only, not improved by glasses; his fields were greatly contracted; the papillae were greyish white, atrophic and excavated; the retinal vessels were extremely narrowed and scanty, and there was a glaucomatous halo surrounding the papillae. The author gives a beautiful coloured plate of the fundus, showing all the features of a severe retinitis pigmentosa combined with glaucoma. His parents were living and were unrelated; they had good vision. A sister, aged 16, had myopia of 12 D. and a not very advanced retinitis pigmentosa; she had not suffered from night-blindness. Three other living siblings were normal. The grandparents were unrelated. No consanguinity. Bibl. No. 196.

Fig. 250. *Ayres' Case.* II. 1, aged 37 years, had noticed a defect in his vision commencing at the age of 18; he was unable to go out alone at night, and also had some difficulty in daylight. On examination

it was found that R. V. = L. V. = $\frac{15}{50}$; fields were much contracted; retinal vessels were narrowed; papillae were rather pale and the retinae were moderately pigmented; he was under observation for several years, and the disease progressed slowly; he was also partially deaf. II. 2, aged 35 years, had eyes similarly affected, the onset in her case occurred at about the age of 18; the condition was more severe in her case than in that of her brother and was further complicated by glaucoma in both eyes; she was quite deaf. II. 3, aged 33, had had defective vision since "boyhood," but the condition had remained stationary for several years; he was unable to walk alone at night and had difficulty in daylight; his fields were contracted; R. V. = $\frac{15}{70}$, L. V. = shadows of hand downwards and inwards; he had attacks of acute glaucoma in both eyes for which a double iridectomy was performed with no improvement to the left eye. II. 4 died, aged 16 years, having developed so far no defect in her vision. II. 5, aged 26 years, had normal vision. The parents were living and in good health; the father had normal eyes and the mother with a correction for 6 D. of myopia could see well. No consanguinity. Bibl. No. 138.

PLATE XXI. Fig. 251. *Goldzieher's Case.* II. 1, seen at the age of 30, had always had weak eyes, but had been able up to a year before to earn her living as a sempstress, since then she had had headaches and her sight had become so dim that she was unable to go about alone. She was a strongly built person but was deaf; R. V. = 0, on the left side she was still able to count fingers in certain positions at a distance of a metre; field of vision was very small; the pupil was irregularly dilated almost to the maximum degree; there were cataracts in the posterior layers of both lenses and also bilateral very fine opacities in the vitreous; there was a deep glaucomatous excavation of the papilla; the retina showed in places atrophy of the pigment epithelium and wholly typical star shaped pigmentary deposits at the periphery; tension was raised in both eyes and the condition was diagnosed as bilateral glaucoma with typical pigmentary degeneration of the retina. Her sister, an intelligent midwife, stated that her parents were healthy and unrelated and that of their eight children six (four brothers and two sisters) suffered from night-blindness, and in some cases sight had become so bad as to interfere with their work. One of the brothers was examined and was found to be deaf and to have typical retinitis pigmentosa. No consanguinity. Bibl. No. 193.

Fig. 252. *Pagenstecher's Case.* II. 1, a girl aged 20, was deaf and night-blind in her right eye only; her right field of vision showed a marked concentric contraction, the papilla was white and there was diffuse pigmentary disturbance and atrophy of the choroid; pigmentary deposits in the retina were almost completely absent. The mother, I. 2, had three sisters who suffered also from deafness and night-blindness. The author believed that the condition in II. 1 was primarily a choroidal affection and the name of retinitis pigmentosa for it had been ill-chosen. We include it under the title of chorio-retinitis. No consanguinity recorded. Bibl. No. 44.

Fig. 253. *Bullar's Case.* "Deficiency of the choroid" in a boy aged 16 (1892). II. 1 had always had bad sight; refraction myopic, 5·5 D.; R. V. with correction = $\frac{6}{18}$, L. V. = $\frac{6}{12}$; seen again in 1898 when his myopia was 7 D.; fields consisted of a small central area of less than 10°, and of a peripheral part about 10° wide lying between the 50° and 60° circles; greater part of fundus was greyish-white with scattered pigment spots, red reflex being limited to a small patch at macula region and round the disc; some isolated choroidal vessels were seen at the periphery where there was a faint red tinge. Two sisters and two brothers had good sight, two brothers had bad sight. No mention of night-blindness in the patient or his brothers. No consanguinity. Bibl. Nos. 199, 251, p. 376.

Fig. 254. *Goldberg's Case.* The author describes this as a case of choroideremia in a brother and sister aged 20 and 12 years respectively; he describes a complete absence of choroid at the periphery, so that the membrane was represented by an irregular ring varying in breadth; in the boy there was also an absence of choroid surrounding the disc; he had a nuclear opacity of both lenses. Such eminent authorities as de Schweinitz, Zentmayer and Usher are doubtful of the correct classification of this case. (See Bibl. No. 301.) No further information is given. No consanguinity. Bibl. No. 290.

Fig. 255. *Alexander's Case.* Choroideremia in two brothers, the younger of whom was aged 31 years at the time of examination; he had been night-blind as long as he could remember, and complained of contracted fields of vision and of a ring scotoma; the defects of vision in both cases were very slowly progressive, but the central vision of II. 2 was, with a slight correction for myopia, still quite good at the time of examination. The fundi were quite white except in the macular regions and in spots at the periphery; the discs showed no appreciable amount of atrophy, the retinal arteries were slightly narrowed in II. 2 and more markedly so in his elder brother; lines of pigment, anterior to the retinal vessels, were described stretching across the fundi and producing a cobweb appearance. The elder brother had a posterior capsular cataract; varying amounts of deafness were present in the family. Nine siblings were all very well developed and healthy, the mother had a brother and a cousin who complained of bad sight especially in a dim light, and a nephew with weak sight. No consanguinity. Bibl. No. 265.

Fig. 256. *Dor's Case.* Chorio-retinitis affecting four siblings. The disease in each case was first noticed at about the age of 30 and was then characterised by night-blindness with spidery pigmentary lesions; then followed the appearance of round choroidal plaques scattered over the fundus; later white fibrous lines were to be seen in the retina; adhesions between the iris and lens next occurred, and lastly, cataract,

and almost complete blindness towards 50 years of age. The condition was not modified by treatment with mercury or salicylate and the patients were in other respects normally constituted, with no history of syphilis or tubercle in them or their parents. III. 2, aged 47, was almost blind and had two children aged 18 and 10 years (1910). III. 3, aged 45, had night-blindness and chorio-retinitis. III. 5, aged 43, was affected and had two living children aged 14 and 7½ years respectively. III. 6 died, aged 24. III. 8, aged 38, was normal and had a child aged 15. III. 9, aged 36, was normal. III. 11, aged 33, was affected and had two stillborn children. III. 12, aged 26, had not yet developed the disease. There is a history of sudden death and heart disease in former generations; thus I. 2 died suddenly (age unknown), also I. 11, aged 30; II. 1, 2, 3, 4 and 6 all died suddenly, II. 1 at age of 40, II. 2, aged 70, II. 3, aged 50, II. 4, aged 73, and II. 6 at the age of 45. The family attributed the trouble in gen. III. to dampness of the house, the members who did not develop the disease had lived elsewhere. No consanguinity. Bibl. No. 267.

Fig. 257. *Pöllot's Case.* Atypical chorio-retinitis and retinitis pigmentosa in the same pedigree. III. 2, Walter H., a student, aged 18, was night-blind and for a long time had been aware of blanks in his fields of vision and of dimness of vision; he was bodily and mentally healthy and had previously been diagnosed as having retinitis pigmentosa. On examination the chief features of the ophthalmoscopic picture consisted in a diffuse atrophy of the pigment epithelium, diffuse sclerosis of the choroidal vessels, and pigmentation in the periphery of the retina similar to that of retinitis pigmentosa; the papilla was of a greyish red colour, the retinal vessels narrower than normal; the choroidal vessels were seen to be of a yellowish colour indicating a high degree of sclerosis; in the macula regions were irregular reddish flecks and towards the periphery were many yellowish white patches; contraction of fields and the presence of scotomata were demonstrated; R. V. with $-2{\cdot}5$ D. $=\frac{5}{10}$, L. V. with $-3{\cdot}0$ D. $=\frac{5}{10}$.

It was reported that his elder brother had the same affection and had been relieved from military service on account of his eyes. A younger brother died aged 10 months.

The father of the sibship, his six siblings and his parents all had normal vision.

The mother, Frau Rosa H., II. 3, aged 46, had always seen badly and particularly so in the evening; R. V. = L. V. with $+3{\cdot}5$ D. cyl. $+0{\cdot}75$ D. axis h. $=\frac{5}{7{\cdot}5}$; fields were normal, no scotomata were present; the papilla was waxy and of a greyish red colour, the retinal vessels narrower than normal; the fundi at the periphery showed fine deposits of pigment typical of retinitis pigmentosa.

II. 4, the twin sister of II. 3 and aunt to the sibship III. 1–3, had been examined by Leber some years previously who reported that her fields were normal in daylight, she was not noticeably night-blind, V. $=\frac{6}{15}-\frac{6}{10}$, and deposits of pigment at the periphery of her fundi were typical of retinitis pigmentosa.

These twin sisters had three normal half siblings and nine normal half nieces and nephews as a result of the second marriage of their mother who had normal eyes but died aged 53 of "consumption." Their father, I. 4, died aged 46, of "consumption and pleurisy"; he had always seen very badly and was almost blind at the time of his death. Their uncle, I. 3, had to give up his work at an early date on account of his eyes and had very weak sight to the end of his life.

II. 4 married II. 5, who was short-sighted but otherwise normal, his parents and his brother also had normal eyes. They had four children, of whom one son died aged 10 months; a son, aged 11, had meningitis at the age of 6 months and was backward bodily and mentally; William W., aged 22, III. 5, had always suffered from night-blindness, he had been examined by Leber at the age of 8 years who found V. $=\frac{6}{20}-\frac{6}{15}$, fields slightly contracted, severe night-blindness, a number of large confluent patches of atrophy of the pigment epithelium in the neighbourhood of the disc with a marked development of pigmentation in the periphery; he was diagnosed as atypical retinitis pigmentosa. When examined 14 years later the condition was similar to that of his cousin, III. 2, and he was diagnosed as atypical chorio-retinitis pigmentosa with marked night-blindness, contraction of fields and ring scotomata. The eldest son, Otto W., aged 25, was night-blind, his fields had normal boundaries but small scotomata were present; the papilla was a good red colour, the retinal vessels of normal calibre, the macula regiou was of a dark brownish black colour and there were no very definite changes in the fundus.

III. 5 appears to have been delicate and to require a good deal of nursing as a child but otherwise there is no mention of other physical disabilities in this family. No consanguinity. Bibl. No. 277.

Fig. 258. *Oguchi's Case.* Night-blindness in five siblings, only one of whom was examined, a young man who possibly was a case of choroideremia. He, III. 2, was first noticed to be night-blind at the age of 6; his daylight vision was normal, colour sense was normal; fields in a bright light were normal, in a dim light were markedly contracted; light sense was defective; ophthalmoscopic examination showed the papilla and retinal vessels to be normal, there was a diffuse uniform greyish white coloration of the fundus in the equatorial and peripheral regions; the retinal vessels stood out in relief very prominently against the pale background and there was a marked white reflex along the course of the vessels. The choroidal vessels could only be seen in the periphery. In the right fundus, in the upper temporal periphery there was an elliptic patch almost the size of the disc, of a dark brown colour surrounded by a whitish grey reflex, lying between two arterial branches. There were numerous deposits of pigment to be seen. The patient was healthy with no history of syphilis; his eldest sister, aged 24, suffered from night-blindness as also did

his younger brothers, aged 17 and 12 respectively, and a sister, aged 7; it was not known whether his youngest sister, aged 4, was also affected. There was apparently another sibling whose condition is not mentioned.

The parents were first cousins, the two grandfathers being brothers. There was no knowledge of syphilis in the parents. It is a misfortune that there was no ophthalmoscopic examination of the night-blind siblings. Consanguinity. Bibl. No. 283.

Fig. 259. *Oguchi's Case.* Night-blindness in four brothers with probably choroideremia in one of them, the only case unfortunately which could be examined; several sisters had normal vision. The patient, Nagajama, aged 20, believed that his night-blindness, which was severe, had remained unchanged since childhood. On examination it was found V. R. = V. L. = $\frac{6}{12}$; fields were contracted to 50°; media were clear; papilla and retinal vessels were normal, the latter appearing dark and distinct to the finest twigs, in contrast to the greyish white fundus which was almost uniform from the papilla to the equator except for clearly defined patches here and there which showed the normal fundus colour; these patches were usually at the bifurcation of vessels and might be of the size of the disc; at the outermost periphery the fundus had its normal colour but not uniformly so. No consanguinity. Bibl. No. 283.

Fig. 260. *Koenig's Case.* (Taken from Nettleship.) Choroideremia in two brothers. III. 1, aged 20, asked for exemption from military service on account of night-blindness from which he had suffered since his earliest recollections; he could read small print accurately, but not easily, in a rather dim light; colour vision was good; fields a little contracted in full light, became extremely contracted on lowering the light; discs were normal, retinal vessels normal; over nearly the whole fundus in each eye the reflex was quite white from absence of choroidal tissue, but the yellow spot region, where the chorio-capillaris was still present, was of a more or less normal red colour; a few large choroidal vessels could be seen and a few pigment patches were present behind the retinal vessels at the periphery. A younger brother was similarly affected and his fundi presented almost exactly the same appearance except that in his case pigmentary deposits were rather more numerous. III. 1 was the eldest of a sibship of nine of whom seven were normal. Parents and grandparents saw quite well. No consanguinity recorded. Bibl. Nos. 86, 251, p. 375.

Fig. 261. *Oguchi's Case.* III. 3, seen aged 21, was the son of first cousins whose fathers were brothers, he had been night-blind since childhood, had normal vision in good daylight, and normal colour sense; his fields, in a bright light normal, became contracted in a dim light; his papilla was normal but was surrounded by a thick black ring; the fundus was of a whitish grey colour and the retinal vessels appeared dark and distinct on the pale background so that the smallest twig could be seen; the macula region was dark. The author gives a coloured plate of the fundus which is suggestive of choroideremia.

The patient's four brothers and one sister had normal vision, but a son of his father's elder brother, aged 25, was said to suffer from night-blindness. Consanguinity. Bibl. No. 283.

Fig. 262. *Zorn's Case.* This is an extremely interesting pedigree showing choroideremia, ? gyrate atrophy of the choroid and retina and atypical retinitis pigmentosa in three generations. I. 1 was not examined, she was reported to have suffered with her eyes since her youth and to see especially badly in a dim light, she could not find her way about in the dark. She had three children, of whom II. 2, Otto A., aged 39, was absolutely helpless in the dark and was dazzled on going from the dark into the light, he had been night-blind since childhood but thought his eyes were getting worse; R. V. with −2·5 D. = $\frac{5}{\infty}$ nearly, L. V. with −1·5 D. = $\frac{5}{\infty}$; fields were contracted to 20° and the whole of the L. upper temporal quadrant was missing; media were clear, papillae normal and retinal vessels were normal; the fundus was almost completely white, with some pigment deposits and choroidal vessels showing in places, at the yellow spot was a brownish black pigment fleck about half the size of the papilla; a coloured plate is given of the left fundus. II. 3, aged 33, may perhaps be described as a case of chorio-retinitis pigmentosa, she had some difficulty in seeing at night; R. V. = L. V. = $\frac{5}{5}$; fields were contracted to 10°—20°; media clear; papillae and retinal vessels normal; in the periphery of the fundus were atrophied patches of a yellowish white colour and pigment deposits. II. 5, the third child of I. 1, was normal.

II. 2 had seven children, of whom six were normal and one, Gertrude H., aged 13, had been night-blind since childhood; R. V. = $\frac{5}{6}$, L. V. = $\frac{5}{7}$; some hm.; fields contracted 40°—70°; the fundus was absolutely normal; possibly a case of retinitis pigmentosa *sine pigmento*. II. 3 had one child, a boy, aged 9, Walter H., who had been noticed to be night-blind for several years; R. V. = L. V. = $\frac{5}{7}$; fields contracted to 10°—20°; papillae and retinal vessels normal; in places the fundus is said to be completely white and pigmentation of the periphery is described but the condition is not typical of the condition described by Fuchs as gyrate atrophy of the choroid and retina. II. 5 had four children, of whom three were normal, and one, III. 8, Franz Z., aged 16, was night-blind; R. V. with −1·0 cyl. axis 0° = $\frac{5}{5}$, L. V. with +1·0 cyl. axis 90° = $\frac{5}{5}$; fields were contracted to 10°—20°; media were clear, papillae and retinal vessels normal; the whole fundus showed a diffuse atrophy of the pigment epithelium except at the macula region, and pigmentary deposits are described in the anterior layers of the retina. All members of the family were healthy and free from defect except in their eyes. No consanguinity recorded. Bibl. No. 323.

Fig. 263. *Tatham Thompson's Case.* Choroideremia in a youth, aged 18 (1898); a great-uncle, I. 3,

suffered badly from night-blindness and was said to have had similar eyes to the patient. III. 1, from his early infancy, had been noticed to hold objects close to his eyes, and to peer round at things as if he only saw straight in front; he had my. 3 D.; corrected vision for each eye = $\frac{6}{9}$; fields of vision were contracted to less than 10°; the fundus everywhere was dazzling white with retinal vessels coursing over, except at the macular region where chorio-capillaris were present and produced a red reflex; a single spot of pigment was visible; the retinal vessels were normal or slightly undersized; O. D. was pale pink in contrast with surrounding white; the condition was unchanged when seen again in 1904. Parents had good vision, they had eleven children of whom three died in infancy; no history of syphilis or tubercle. The author gives a pencil sketch of the fundus. No consanguinity. Bibl. Nos. 208, 251, p. 376.

Fig. 264. *Jackson's Case.* II. 1, aged 35, had always had defective vision and it had slowly become worse; V. = $\frac{4}{40}$; she was not night-blind; the retinal vessels were rather small; the whole central portion of the fundus showed choroidal atrophy with disturbance of pigment epithelium, the condition shaded gradually from complete atrophy at the centre to practically normal fundus at the periphery; there were relatively large pigment patches near the centre and minute brown specks were visible throughout the fundus; a coloured plate is given of the right fundus. II. 4, the youngest but one of the sibship, was examined by Dr Gratiot who reported that her eyes were like her sister's but that in her case the condition was more severe. Two brothers died young, one of them of diphtheria in infancy and the other at the age of 7 years from pulmonary affection, four sisters had good sight. The parents were third cousins. Consanguinity. Bibl. No. 233.

Fig. 265. *Wernicke's Case.* Gyrate atrophy of choroid and retina in a youth, aged 22, the youngest of a sibship of 10; a sister eight years older than he, probably was a similar case, for she was night-blind, had always seen badly and the surgeon who operated on her for cataract, which was bilateral, told her that she had a congenital defect of the fundus. II. 3 had always seen badly, he was night-blind and had small anterior polar cataracts; his papilla was normal and the retinal vessels were not narrowed; the fundus, over an area surrounding the papilla, was white, showing atrophy of the choroid, beyond this area was an irregular ring of normal fundus which again was surrounded towards the periphery by an area showing atrophy of the choroid. A very detailed description of the fundus is given by the author. The father died suddenly, aged 59; the mother was healthy and had normal eyes. No consanguinity. Bibl. No 256.

Fig. 266. *Fuchs and Cutler's Case. Atrophia gyrata chorioideae et retinae* in three sisters, the offspring of first cousins; their four brothers, aged 23, 20, 16 and 12 respectively, all had normal vision; three siblings had died young, two of them from diphtheria. The father was dead, but was believed to have had normal vision, the mother was examined and found to have normal eyes; there was no inherited or congenital eye disease known in the family of either.

II. 2, Gisela Geyer, aged 26, had R. V. with -18 D. = $\frac{5}{24}$, L. V. with -20 D. = $\frac{5}{24}$; fields were considerably contracted; there were small almost round opacities at the posterior pole of both lenses; she had no strabismus; on examination of the fundus there was found a large staphyloma surrounding the disc with peculiar lobulated protrusions into a zone of normal fundus, further towards the periphery there was a uniform zone of atrophy. The edges of the staphyloma and of the atrophic zone were sharp in outline and partially marked out with pigment; the fundus between them was quite normal. The atrophic zone appeared almost uniformly white with a very few choroidal vessels near its inner margin, towards the periphery it was covered with a dense network of black pigment. Both fundi were similar. She was subject to fainting fits, was married, and had three boys who saw well.

II. 3, Irma Prohaska, aged 24, had vision which was reduced to perception of light; at the age of 11 she suffered from night-blindness and had strabismus; she had opacities in anterior and posterior cortical layers of both lenses; her whole fundus showed an atrophic choroid except at one place outwards from the papilla where an area two or three times the size of the disc was red and surrounded by black pigment, some deposits of pigment were scattered over the atrophic areas; the discs showed a high degree of atrophy.

II. 5, Rose Prohaska, aged 21, had R. V. = finger counting at 2 m., L. V. with -10 D. = $\frac{5}{60}$; the right field was considerably contracted and the left slightly so; she had been night-blind for five or six years; she had strabismus of right eye and posterior polar cataracts in each lens; on the right, the papilla was surrounded by a staphyloma which was continuous at one point with a peripheral atrophic zone, on the left the staphyloma was nowhere connected with the atrophic zone; the main features of her fundi were the same as in the case of II. 2. Consanguinity. Bibl. No. 177.

Fig. 267. *Laurence and Hutchinson's Case.* This case, first described by Laurence in 1866, is believed to be the same family as the case described by Hutchinson in 1900; it has been placed by Nettleship and Usher under the heading of "*Atrophia gyrata chorioideae et retinae.*" The following description is taken from Nettleship's account of the case, for he discussed the case with Hutchinson and took some pains to try and remove the minor discrepancies which exist between the two accounts of the family. Hutchinson gives a coloured plate of the fundus in the case of II. 12, a girl, aged 16 when the drawing was made, whose sight began to fail about the age of 5 or earlier; a narrow zone of choroid immediately around the optic disc appears quite natural; then comes a very broad zone of incomplete atrophy, leaving only the large vessels, and even they are converted into white bands; about the equator the choroid becomes

gradually less atrophic, although the pigment epithelium and chorio-capillaris appear to be universally absent; some angular and stellate pigment deposits are present in the retina, but not very characteristic either in form or distribution; retinal vessels are stated to have been normal, but when seen again in 1876 they had become shrunken and the discs wavy, although there was no increase of pigment. When seen by Laurence in 1865 she was aged 7; there were already scattered irregular black deposits in the retina of various shapes, but mostly angular, branched or linear, and all the choroidal vessels were very plainly visible, the inter-spaces being paler than the vessels. Laurence described her irides as grey and hair light auburn, her sight as very defective and much worse at night, and her intelligence as dull. When last seen by Hutchinson (1876) she was about 18, had not begun to menstruate, was very nervous, and was considered by her mother to be losing power in her legs; she was the youngest in a sibship of ten. II. 2 was normal and has two normal children; II. 4, a fine man, had five normal children. II. 5 began to lose power in his legs at the age of about 4 years, and became paraplegic, is mischievous and passionate and had to be under care; at the age of 20 Laurence found him only 5 feet $3\frac{1}{4}$ inches high, obtuse in intellect since childhood, sight very defective especially after dusk, muscular power of legs very defective; fundi showed diffuse incomplete atrophy of choroid, absence of pigment epithelium, and a few scattered pigment spots; in fact, Laurence's description of this young man's fundus might almost be applied to Hutchinson's illustration of the sister's eye. II. 6, pitted by small-pox, was 4 feet $6\frac{1}{2}$ inches high when aged 18, legs semi-paralyzed; sight began to fail at about the age of 6, especially at night; fundi show changes like those in the other cases, but the choroidal atrophy was much more advanced, "the fundus has the appearance of a diffused staphyloma posticum." Hutchinson found much the same 10 years later. II. 7 died of small-pox aged 6 weeks. II. 8, 4 feet $4\frac{1}{2}$ inches high, was dull and inanimate like the other affected brothers; legs not so weak as in the other cases and he could run about well till the age of 6 years; vision failing since the age of 12, worse at night, fundi as in II. 5. II. 9, seen aged 22, was normal. II. 10 died of whooping cough at the age of 2 years. II. 11, seen aged 18, was normal. Refraction was hypermetropic in all the affected members; fields of vision stated to be apparently of full size, but there was nystagmus and eccentric fixation.

In all the affected males, development of the sexual organs was arrested, being, according to Laurence, no larger and less perfect than those of a child of 12 months.

The mother of this sibship was normal, she was the only child of parents who died young and knew of no nervous disease in her relatives. The father died suddenly after a sort of fit at the age of 52, he had had no serious illness but had always been very nervous, had much headache in the last years of his life with occasional pains in his limbs, especially on the left side, and for a month or two before his death there was numbness in his left foot; he was a well built man with good vision. The father had three normal brothers who had no children, and two sisters who were normal and had normal children. No consanguinity. Bibl. Nos. 55, 212, 251, pp. 371—3.

Fig. 268. *Jacobsohn's Case.* Probably gyrate atrophy of choroid and retina in father and son. III. 1, aged 20, had been night-blind since very early life; fields were very small; V. = $\frac{20}{100}$ and smallest print at 3 to 5 inches; discs and retinal vessels as in retinitis pigmentosa; the choroid was healthy over a large area including the disc and macula region, anterior to this was a zone over which large areas of the choroid were atrophied, its vessels sclerosed and the overlying retina abundantly pigmented. A coloured plate is given of the fundus. The patient was physically and mentally weak. His father, aged 48, had also been night-blind from earliest life and had a similar fundus, his condition had progressed and he had been quite blind for a year and a half. The mother, aged 54, had incipient cataract, myopia of 1·5 to 2 D. and a normal fundus, V. = $\frac{20}{30}$ in each eye. The grandparents were healthy and unrelated, a sister of the mother was very 'short-sighted.' No history of syphilis.

III. 1 had four siblings of whom two died in infancy, a boy died aged 8, and a sister aged 15 had normal vision. No consanguinity. Bibl. No. 155.

Fig. 269. *Van Duyse's Case.* Retinitis punctata albescens in three siblings. (Two excellent coloured plates of the fundi are given by the author.) II. 1, Josephine L., aged 20 years, had suffered from an extreme degree of night-blindness since the age of 2, and her light sense had become so reduced that it could not be measured by Förster's photometer, her vision was reduced to finger counting at 3 metres; colour sense was defective; she had slight horizontal nystagmus; she had black hair, brown irides, and had good general health; fields of vision were concentrically contracted; teeth were good and urine normal; the fundus showed slightly narrowed arteries with normal veins, the choroid was very dark with some yellowish patches at the periphery as wide as the large retinal veins, and there were present innumerable minute white dots over the whole fundus, but most abundant near the disc and less so in the macula region; the retinal vessels passed in front of the white spots. II. 2, Arthur, aged 19, was normal and healthy in all respects. II. 3, Maria, aged 18, had slight myopia and a normal fundus. II. 4, Auguste L., aged 12, was in an institution for the blind, he had suffered from very marked night-blindness since the age of 4 or 5 years; his fields were concentrically contracted; he had a horizontal nystagmus; he was myopic (R. 7·5 and 6·5, L. 8 and 5·5, normal axes); corrected vision = $\frac{1}{8}$; and his fundus was as in his sister's case sprinkled with white dots, the retinal arteries being narrowed and the choroidal trunks showing some selerosis at the

periphery. II. 5, Louise, aged 7, had a normal fundus. II. 6, Raymond L., aged 5, was in an institution for the blind; he had shown evidence of very marked night-blindness since he first walked; his fields were greatly contracted and he had horizontal nystagmus; he was a very intelligent child; his fundus was sprinkled with white dots like those of his elder siblings, but they were the most abundant in his case at the periphery; there was sclerosis of some of the choroidal trunk vessels. There was no trace of pigment to be seen in the fundi of any of these cases. The father, aged 44, had normal vision, as also had the mother, aged 42. The mother had had four other children who had died in infancy of pneumonia, "dropsy," or croup. There was no history of syphilis. No consanguinity. Bibl. No. 241.

Fig. 270. *Lauber's Case.* Retinitis punctata albescens in four out of six siblings. The condition in this family was characterised by night-blindness with ophthalmoscopic changes; the fundi were covered with minute white spots which were absent only in the macular region over a limited area and were situated deeper than the retinal vessels, the discs and retinal vessels were normal; colour vision was normal except for some slight anomaly in the case of one boy; the fields were normal in a good light but considerably constricted in a dim light; the condition, the author considered, was evidently stationary. The sibship consisted of II. 1, male, aged 28, affected; II. 2, male, aged 25, examined and found normal; II. 3, male, aged 19, affected; II. 4, female, aged 15, affected; II. 5, female, aged 9, normal; and II. 6, female, aged $5\frac{1}{2}$, affected. The parents were first cousins once removed, the father, aged 56, was examined and found normal, the mother was not examined but was said to have normal eyes. Consanguinity. Bibl. No. 260.

Fig. 271. *Gayet's Case.* III. 2 had always suffered from night-blindness and been unable to go about alone after sunset or in a dimly lit room; he had been passed for military service and was urging his visual difficulties. He was found to have good central vision but contracted visual fields and very defective colour vision; the papillae were a little redder than normal, the retinal vessels a little narrowed, and there were an immense number of white spots covering the whole fundi from papilla to periphery, but less abundant and smaller in size in the papillary and macular regions; there were no pigmentary deposits and the retinal vessels passed in front of the spots; the retina had a greyish opalescent tint; he stated that his eyes were as they had been in infancy. He was not deaf but had no perception of shades of sound. III. 4, aged 13, sister to III. 2, presented a similar condition but in her case the white spots were less numerous, especially in the left fundus, and in the peripheral regions she showed changes characteristic of true retinitis pigmentosa; she also had very defective colour vision and no perception of shades of sound.

Two brothers and a sister, the first, third and fifth members of the sibship, had normal vision. The parents were healthy first cousins. A maternal uncle had very bad sight and the maternal grandfather was blind for several months before his death at the age of 70. Consanguinity. Bibl. No. 120.

Fig. 272. *Spengler's Case.* Nettleship considered this an atypical case of retinitis punctata albescens and the accompanying coloured plate poor. The parents and grandparents were healthy and had good sight; the two grandmothers were first cousins. III. 5, aged 12, was very fair, she had slight convergent strabismus and horizontal nystagmus; her light sense was very little reduced; colour sense normal; fields showed very little contraction even in a dull light; media clear; the papillae were a light yellowish red colour with no excavation; retinal vessels normal; the fundus was albinotic with dark irregular pigmentation of the macula region; the whole retina was covered with "thousands upon thousands" of white dots; there were also in the choroid larger yellowish spots of different sizes and shapes. The same description applies to III. 4, a boy aged 13. III. 3, aged 15, had a completely albinotic fundus with the same white spots but no yellow patches in the choroid; she also had patches of pigment at the periphery quite unlike those of retinitis pigmentosa. III. 2, aged 16, had ashy fair hair and a fundus similar to her younger siblings with no yellow patches in the choroid and fewer white spots. None of the siblings had contraction of visual fields or night-blindness. Consanguinity. Bibl. No. 216.

Fig. 273. *Griffith's Case.* II. 2, a silversmith, aged 48, came up complaining of night-blindness from which he had suffered all his life; there was no history of syphilis; his parents were first cousins; his sister, who also suffered from night-blindness, married her first cousin and had a son whose sight was normal. The author found R. V. = L. V. = $\frac{6}{36}$, not improved by glasses; the patient showed a marked deficiency in light sense, with fields which though normal for white and for colours in a good light became markedly reduced for colours in the slightest shadow; he had no central or ring scotoma; colour vision was normal; the discs were pale and somewhat waxy, the retinal vessels slightly constricted; there was a general mottled condition of the whole fundus but especially round the disc and macular region where there was a ring area covered with discrete yellow spots resembling Tay's choroiditis. Nettleship reports that the description of the spots is not quite characteristic, but that in all other respects the case is typical of retinitis punctata albescens. Consanguinity. Bibl. No. 195.

Plate XXII. Fig. 274. *Nettleship's Case.* Retinitis punctata albescens in two siblings. This history is of great interest as being one of the very rare cases in which typical retinitis punctata albescens has been seen to lose all its white dots. VI. 2, aged 21 (1887), was a healthy lad working on his father's farm; as long as he could remember he had been unable to see well in the dusk; with slight hm. as. corrected R. V. = $\frac{6}{9}$, L. V. = $\frac{6}{12}$; at posterior polar area were numerous single minute very white dots, evenly dis-

tributed and free from pigment, reaching close up to the fovea; the subjacent choroid looked perfect anteriorly the spots thinned off, but there the epithelium became disturbed and choroidal trunks visible; further towards the periphery the choroid was even paler and showed a little granular pigmentation; the discs were slightly hazy, the retinal vessels normal; there was nothing like retinitis pigmentosa anywhere; fields in daylight were reduced by 10°—15°, in dim light they were reduced to the 20° circle. The patient was seen again in 1894 and 1905 when no change had occurred but he thought that he adapted to changes of light less quickly. In 1913 VI. 2, now aged 47, was examined and *no white dots could be found in any part of either fundus*; disturbance of the hexagonal epithelium is described, also exposure of the choroidal vessels most marked in the lower part of each fundus, where in the R. were seen three definite pigment patches of characteristic bone corpuscle pattern; in the L. were several smaller patches of pigment not of the typical shape; the discs were pale and hazy, the retinal vessels perhaps slightly diminished, lenses and vitreous clear, vision as before.

One younger sister, VI. 8, aged 32 (1905), had the same condition, she had been night-blind since childhood; R. V. = L. V. = $\frac{5}{36}$; fields, in daylight full, were contracted in a dull light; the ophthalmoscopic appearances resembled those in her brother but the white dots were smaller and much more numerous. In 1913 the white dots were much less abundant, there were no pigment spots or patches in either eye, but the discs were markedly paler than her brother's and the arteries were very considerably shrunken; she said that her sight was no worse.

Of their siblings VI. 1 had hare-lip, VI. 3 and 6 died, aged 5, VI. 4 died in infancy, VI. 7 had hare-lip and died in infancy, VI. 5, 9 and 10 were normal. The parents were first cousins once removed. VI. 2 was born at 7 months and was only 9½ months younger than VI. 1. Consanguinity. Bibl. Nos. 251, 299, pp. 387—9.

Fig. 275. *Collins and Nettleship's Case.* Retinitis punctata albescens (?) and retinitis pigmentosa in four siblings, three of whom have been examined by four ophthalmic colleagues at one time or another. The parents and grandparents on both sides were first cousins. Of the eight normal siblings, two died young, one of "water on the brain."

III. 1, aged 38 (1896), had noticed night-blindness for four or five years; refraction nearly em.; R. V. = $\frac{6}{18}$ partly, L. V. = $\frac{6}{12}$ partly; media clear; numerous fine, dull, white dots, chiefly at the periphery of the fundus, were described; discs were healthy, retinal vessels a fair size, fields contracted. A different surgeon in 1905 reported discs rather pale, retinal arteries too small, no pigment deposits, vision as before. Her brother, III. 2, aged 43 (1905), had noticed night-blindness for a year or two; slight hm. as. corrected gave R. V. = $\frac{6}{5}$, L. V. = $\frac{6}{6}$; definite retinitis pigmentosa of typical character was described at the periphery of both eyes; discs rather pale, retinal arteries too small. One of his children, a girl aged 11, was examined and found to have normal eyes. III. 4 was reported to be night-blind, but was not seen. III. 5, aged 20 (1895), was night-blind and intellectually dull; he had no retinitis pigmentosa, but at the periphery of the fundus were numerous discrete white spots; he died young of phthisis. In this family the white dots were confined to the periphery and night-blindness was not noticed until about 20 to 30 years of age. One of them, III. 2, with typical retinitis pigmentosa and no white dots, only noticed his night-blindness at the age of about 40. Consanguinity. Bibl. No. 251, p. 391.

Fig. 276. *Nettleship's Case.* Two sisters with retinitis punctata albescens. IV. 1, aged 19 in 1886, was seen again in 1901, 1907 and 1913; she had been night-blind all her life; hm. of 3·5 D.; vision and fields were normal in a good light but her fields were contracted by artificial light and light sense (Förster's photometer) was very defective; she was thin and delicate-looking from overwork. At the fundus of each eye an immense number of minute discrete dead-white dots were present at the equator and extended nearly as far back as the disc; the discs and retinal vessels were normal. In 1913 the night-blindness was no worse and ophthalmoscopic appearances were much as at the examination twenty-seven years before; there were no dots at the yellow spot and none at the periphery though the epithelium at the periphery had a granular appearance. IV. 4, aged 14 (1887), was seen again in 1892 when her condition was unchanged; she had white dots in her fundus exactly like those of IV. 1 but more numerous, they were wanting in the down-in part of each equator and peripherally to the equator where the stippling of the pigment epithelium was coarsened and ill-defined pale spots, apparently thinned choroid, were seen; at the extreme periphery were some circular dots of the same size but less white than the typical white dots and surrounded by pigment; with + 4 D. V. = $\frac{6}{9}$ partly; she was dusk-blind like her sister; she died aged 29 of phthisis.

Of the siblings IV. 5 was examined and fundi were normal; IV. 2, 3 and 6 were healthy and had perfect sight. IV. 7 died aged 2. The mother had been healthy but died from cardiac failure after pneumonia; two of her siblings died of phthisis. The father died aged 48 of diabetes. No consanguinity. Bibl. Nos. 251 (pp. 385—6), 299.

Fig. 277. *Ulrich's Case.* II. 1, a boy, aged 12, suffered from night-blindness and typical retinitis pigmentosa; the author describes in considerable detail the presence of fine thread-like opacities in the vitreous humour of both eyes which he believed to be the remains of embryonal vessels in the vitreous. II. 2, a sister, aged 8½ years, also suffered from night-blindness and retinitis pigmentosa. II. 3, a sister, aged about 4, had retinitis punctata albescens. No further information or description of her case is given. No consanguinity. Bibl. No. 126.

Fig. 278. *Nettleship's Case.* Retinitis punctata albescens in II. 2, a male, aged 31 (1891). He reported that he had seen badly in a dull light as long as he could remember and that it did not get worse; in a good light he could see perfectly. It was extremely slow adaptation to dull light rather than dusk-blindness; an exposure of only three or four minutes to sunlight would blind him so that for the next five minutes he could not find his pipe in a shady room; after two hours in the afternoon sun in Florida where he had lived he was so blind at sunset that for some time he could not see a man close to him, but after an interval of an hour or less his night-blindness left him and he believed he could see as well as other people. V. R. = V. L. = $\frac{6}{6}$; hm. of 0·5 D.; Bjerrum's types $\frac{6}{12}$ slowly (against the authors $\frac{6}{9}$); characteristic white dots of retinitis punctata albescens were present at posterior part of fundus and as far forwards as equator, they closely surrounded the disc where also the nerve fibre layer of the retina was rather hazy; the yellow spot itself was free from white dots but the retina there showed a fine mottling; the dots often lay parallel to choroidal vessels; no dots were present at lower part of equator and he had once found he could see a little in the upper part of his field when he could not see at all in front; fields were quite full in daylight, contracted in a reduced light. His father had four normal children by his first unrelated wife; by his second wife, who was his first cousin, he had two children, the patient, and a girl aged 29, with perfect eyes. The patient died soon after he was examined in Florida of tubercular meningitis. Consanguinity. Bibl. No. 251, pp. 383—4.

Fig. 279. *Takayasu's Case.* II. 1, a well grown not badly nourished schoolboy, aged 10, was noticed to be night-blind when he was aged 7; on examination it was found that his refraction was emmetropic, R. V. = L. V. = $\frac{6}{6}$, pupils were normal, fields were very slightly contracted, colour sense was normal; his functional defect consisted in a marked lowering of central vision in a dim light; the fundus was covered with very small white points, only the regions of the papilla and the macula lutea remaining free, the spots were mostly round but towards the periphery were sometimes oval, in the equatorial regions the distribution was more scattered, sometimes the spots were confluent, they were always behind the retinal vessels, they were not bordered by pigment and there was no abnormal pigmentation of the retina. The author described him as a case of retinitis punctata albescens.

The parents were first cousins; three younger brothers were healthy but one of them suffered from night-blindness. Consanguinity. Bibl. No. 239.

Fig. 280. *Diem's Case.* Doubtful retinitis punctata albescens in a girl, III. 1, aged 18½ when examined, whose father suffered from a progressive retinitis pigmentosa but had never been night-blind, and whose uncle, II. 1, also suffered from retinitis pigmentosa and was in a home for the blind; II. 1 had seen badly in the dark since childhood. The father had five other siblings who were short-sighted but otherwise had normal eyes and of whom one, a sister, had been deaf since her youth, and another sister was epileptic. The paternal grandmother had been unable to read much at the age of 30, and at the age of 50 was blind to all except the perception of light; she had never been examined. III. 1 had a brother, aged 4, who was not night-blind and had a normal fundus. She herself had never been night-blind but as a school girl had noticed that she did not see so well as the other children; she was myopic and with correction R. V. = $\frac{6}{12} - \frac{6}{8}$, L. V. = $\frac{6}{18}$; her field of vision in full daylight was normal for the R. eye and showed some excentric contraction for the L.; in a reduced light the fields remained unchanged; colour vision was normal; media were clear, the papillae of a rosy colour with clear margin; retinal vessels were normal; surrounding the macula region there was a zone brightly sprinkled with masses of small yellowish white flecks, oval in shape with the long axis radiating from the macula, they were sometimes confluent and the retinal vessels invariably passed in front of them, the inner margin of this zone was clearly defined, the outer was less so, and on the temporal side there were protrusions of the flecked areas into the normal retinal tissues; the macula itself was quite normal. Towards the periphery at a distance of six or seven papilla's diameter from the macula was another zone showing yellowish white flecks of a rather different character, larger in size and more spaced out; beyond this zone the periphery was normal. No consanguinity. Bibl. No. 296.

Fig. 281. *Healy and Drinkwater's Case.* Retinitis punctata albescens in III. 1, a male, aged 23, when examined. He reported that he had had difficulty in seeing in a failing light since his earliest recollections but the disability had increased since he had joined the army. Healy describes how in a darkened room he fell over obstacles and groped his way about; R. V. = L. V. = $\frac{6}{12}$; his fields were contracted to 70° on temporal side, 30° on nasal side; media were clear; the fundi showed hundreds of whitish yellow opaque spots up to 1½ mm. in diameter lying apparently in the deeper layers of the retina, the retinal vessels passed in front of the spots which were superficial to the choroidal vessels; the spots were most numerous in the equatorial zone, fading towards the periphery, they were absent from the macular region and more numerous again in the immediate vicinity of the disc; the fundi were markedly tesselated and several branched collections of pigment were present along the veins in the equatorial zone. The retinal vessels were slightly narrowed, the discs a dirty greyish colour. The author gives a coloured sketch of the fundus.

Drinkwater investigated the family history and reports that the patient's mother, II. 2, her younger brother, II. 3, and her half-sister, II. 6, all had retinitis pigmentosa. The grandparents, I. 1 and 2, were

normal, I. 2 married twice and had affected children by both marriages, he had also two normal sons and three normal daughters by I. 3. II. 3 had eight normal children of whom the eldest was aged 16 years. II. 6 had two apparently normal daughters aged 7 and 1 year respectively. III. 1 had one normal brother.

III. 1 was also partially deaf which appears to have been due to an attack of scarlet fever or measles when he was aged about three years.

No consanguinity recorded. Bibl. No. 324.

Fig. 282. *Cohen's Case.* Retinitis punctata albescens in a sister and brother aged 6 and 13 years respectively; four siblings were unaffected and the parents were normal. This is the only case we have found reported of this condition in a coloured race.

For II. 2, V. $= \frac{2}{40}$, for II. 1, V. $= \frac{2}{70}$. The chief complaint was of night-blindness; no scotomata were present; fields and visual acuity were greatly reduced by diminishing the illumination; the fundi showed numerous discrete greyish white dots with ill-defined borders, varying in size from that of the diameter of a small retinal vessel to that of the disc, arranged concentrically around the equator and spreading towards the periphery; the macular and papillary regions were free from these dots; the retinal vessels passed in front of the dots; and pigmentary changes were present. No consanguinity recorded. Bibl. No. 308 A.

Fig. 283. *Wuestefeld's Case.* Retinitis punctata albescens in a girl aged 8, whose brother, aged 6, had retinitis pigmentosa.

II. 1 was brought up by her father, who stated that she had suffered from night-blindness for some considerable time. On examination it was found that she had myopia of 5 D. and 7 D. respectively in the R. and L. eyes; colour vision was normal; fields of vision were normal in daylight but much contracted in a dull light; light sense (Förster's photometer) $= \frac{1}{30}$. Ophthalmoscopic examination showed that the media were clear; the choroid extremely dark, which was specially striking as she had fair hair; the optic discs were rather pale, the retinal vessels normal; and the fundus presented a multitude of small white dots reaching close to the disc and macula, the smallest being barely visible and the largest equal to about three times the diameter of the retinal vessels in magnitude, no dots were in front of retinal vessels and their number was so great as to give a whitish aspect to the retina. II. 2, aged 6, also suffered in a less degree from night-blindness; he was too young for a complete examination but his choroid also was very dark, without white spots as in his sister and at the periphery there was a typical picture of early retinitis pigmentosa with bone corpuscle-shaped deposits of pigment; the optic discs and retinal vessels were normal. The urine in each case was free from sugar and albumen, and examination for syphilis in the case of II. 1 was negative. The author gives a coloured plate of the fundus of II. 1. No consanguinity. Bibl. No. 217.

Fig. 284. *Galezowski's Case.* Retinitis punctata albescens in two brothers, aged 34 and 21 respectively; a sister, aged 36, had normal eyes, no mention of other siblings between II. 2 and 3. The parents were first cousins and had excellent sight, and the grandparents (? one or both pairs) were also cousins.

II. 2 and 3 were robust with no developmental anomalies, they were noticed to be night-blind as soon as they were able to go about alone. In the case of II. 2 the central part of the fundus was of a greenish brown colour similar to that of Wuestefeld's Case (see Bibl. No. 217); the retina was covered with a multitude of small white spots which were extremely abundant and almost confluent towards the periphery and were less thickly distributed towards the papilla, at the macula none were to be seen; the spots were sometimes round, sometimes oval and there were no deposits of pigment anywhere in the retina; the papilla was rose coloured; the fields were slightly contracted in a good light and considerably more so in a dim light; visual acuity was $\frac{1}{2}$ in ordinary light and was rapidly lowered in a dim light.

In the case of II. 3 the same lesions were present but were less marked, the greenish reflex in the fundus was less marked and the white spots, perhaps a little larger, were less numerous and in parts of the periphery were absent; in his case there were some deposits of pigment typical of retinitis pigmentosa; his fields were less contracted and his vision less diminished than in the case of his brother. Consanguinity. Bibl. No. 231.

Fig. 285. *Cuperus' Case.* III. 2 was suffering from a defect diagnosed by the author as atrophy of the choroid with a high degree of sclerosis of the choroidal vessels diminishing in intensity towards the periphery, with a secondary atrophy of the retina and optic nerve. His two brothers appeared to be similarly affected, the defect appearing in all cases at about the same year of life. Of his four sisters, three were dead and were reported to have had good eyes, one was living and was reported to be short-sighted; she was not examined. The parents of this sibship had normal sight, the grandmother, I. 1, was reported to be blind when she died. III. 2 had seven children, all with good eyes.

III. 2, aged 70, had always been healthy, there was no history of syphilis or nerve disease in the family but he had advanced arterio-sclerosis; he smoked a little and took a little alcohol. His eyes were good until the age of 30 years but since then his central vision had slowly but steadily diminished until he had to give up his work; he had never been night-blind; he was treated by Mooren in 1869 and by Donders in 1874 but received no benefit. At the age of 70 his vision was reduced to finger counting, with excentric fixation; his fields showed absolute central scotomata with normal outer boundaries, the degree of illumi-

nation having no effect upon their size or form; media were normal. The fundi of both eyes were, in the neighbourhood of the papilla and of the macula lutea, a striking white colour; farther out towards the periphery the colour became light brown and in the outermost periphery the normal red colour of the fundus was present. The retinal vessels were small, the smaller retinal vessels having disappeared. The papillae were a light grey colour.

Snellen had examined III. 4 in 1875, he died aged 54; van der Meer examined III. 1 and found a condition exactly similar to that described in III. 2. No consanguinity. Bibl. No. 220.

Fig. 286. *Lindner's Case.* Night-blindness associated with a whitish grey coloration of the fundus in III. 1 the offspring of first cousins, his two siblings died the day after birth and his mother by a second unrelated husband had two normal children.

III. 1, aged 16, had been night-blind since childhood, his colour sense was normal, light sense was much lowered and his fields with normal outer margins in a good light became markedly contracted in a reduced light, there was a small central scotoma for red in the R. eye and a large absolute central scotoma for white in the L. The papillae was blurred but of a normal colour, the vessels were normal; the fundus in the region of the papilla was of a whitish grey colour except at the macula where there was a dark greyish red fleck; the whitish-grey colour extended on the nasal side to a distance of about 6 to 8 papilla's diameter, rather farther on the temporal side and to about half the distance above and below, and the fundus gradually became its normal red colour towards the periphery; the blood vessels stood out very clearly on the white background. Consanguinity. Bibl. No. 298.

Fig. 287. *Mauthner's Case.* This case is of interest as being probably the earliest described case of choroideremia; the following account is taken from Usher (see Bibl. No. 301) as we have been unable to see the author's description of the case:

"II. 1, a male, aged 32, had night-blindness and defective central vision; his condition had got worse after typhus fever fifteen years before; fields were contracted; refraction myopic, R. V. barely $\frac{5}{200}$, myopia $\frac{1}{12}$, L. V. $\frac{10}{40}$, myopia $\frac{1}{16}$; edge of each optic disc was blurred and retinal arteries were narrowed; fundi gave a glaring white-green reflex; occasional choroidal vessels and small pigment heaps were present; a network of vessels in the choroid was present at the macula of the right eye only; macula of the left eye appeared as a well-defined red-brown rhombic area; some lens and vitreous opacities were present in the left eye. The author considered that the choroid was quite absent in the left eye and that there were a few remains of it in the right eye."

His brother, II. 2, had exactly the same kind of bad vision and probably had the same defect; his paternal uncle saw badly. No consanguinity recorded. Bibl. Nos. 78, 301.

Fig. 288. *Mouchot's Case.* Retinitis pigmentosa in a brother and sister, the third and fifth born respectively in a sibship of seven. II. 3, aged 51, had first noticed that he saw badly in the evening fifteen years ago; he was now night-blind and had a concentric contraction of his fields, his central visual acuity was normal; papillae were normal; typical pigmentation of the retina was present in the equatorial region. He had had a history of pneumonia twice and of what was probably a simple conjunctivitis at one time; his six children had good vision.

II. 6, aged 38, also had six normal children; her complaint was of double vision and she had paralysis of the third nerve on the left side; at a later date she was found to have markedly reduced central vision, R. V. = L. V. = $\frac{1}{5}$, concentric contraction of fields and typical pigmentation in the equatorial zone of the retina; she made no complaint of night-blindness and was unaware that there was anything the matter with her eyes except the paralysis for which she was under treatment. Of their siblings II. 2 was an idiot and died aged 7; II. 5 died aged 30 of a pulmonary affection; three sisters were living and well. The parents lived to old age and were normal and healthy. No consanguinity. Bibl. No. 63.

Fig. 289. *Merrill's Case.* (Published by Loeb.) A woman who was suffering from retinitis pigmentosa married and had a son who had coloboma of the iris and choroid. No consanguinity recorded. Bibl. No. 261.

Fig. 290. *Rampoldi's Case.* Retinitis pigmentosa in four brothers, the offspring of consanguineous parents; all the brothers were suffering from pellagra from which disease the mother died. Consanguinity. Bibl. No. 125.

Fig. 291. *La Serre's Case.* This case is of some historic interest though it does not consistently belong to the group of diseases under consideration; it is included here because it has been reported as the earliest recorded case of hereditary night-blindness.

The author writing in 1688 describes a girl aged about 18 years who became night-blind every year about the month of May, the condition lasting for three or four months, after which she recovered and no trace of the defect remained. A paternal aunt and two children of this aunt were affected in the same way. No. consanguinity recorded. Bibl. No. 18.

Fig. 292. *Ovelgün's Case.* This case is of interest as being the earliest recorded case we have found of hereditary retinitis pigmentosa. The author, writing in 1744, was treating II. 1 who came to consult him

and who mentioned that his daughter, aged 14, and his son, aged 2 years, suffered from night-blindness and that the disease was inherited through his wife, she herself being normal, but the sons of two of her paternal uncles being affected in the same way as his own children. The disease appears to have progressed to blindness in one of the cases. No consanguinity recorded. Bibl. No 19.

Fig. 293. *Mouchot's Case.* A single case of retinitis pigmentosa in a sibship of eleven, the offspring of unrelated parents who had good sight. The father died aged 62 and the mother aged 63 of pulmonary affections, the father had been ill for a long time. Two brothers were living and saw well, seven brothers and one sister died between the ages of 19 and 23 years, probably from tubercular affection.

II. 1, aged 25, was completely blind at night; he had first noticed his difficulty at the age of 13; V. R. $= \frac{4}{20}$, V. L. $= \frac{1}{20}$; he had divergent strabismus, tension normal, media clear, fields contracted; his discs were pale, the retinal arteries thread-like and there was typical pigmentation in the equatorial region. The author gives a beautiful coloured plate of the R. fundus. There was no history of syphilis. No consanguinity. Bibl. No. 63.

Fig. 294. *Mouchot's Case.* Retinitis pigmentosa *sine pigmento* in a deaf-mute boy aged 16 who had been night-blind as long as he could remember; he was found to have some contraction of his fields, the discs were normal and his retinal vessels perhaps slightly narrowed. His parents were normal and unrelated; his sister and brother were normal. No consanguinity. Bibl. No. 63.

Fig. 295. *Magnus's Case.* Congenital retinitis pigmentosa in a blind girl whose elder brother also was born blind; one brother was normal. The parents were normal and unrelated. No consanguinity. Bibl. No. 133.

Fig. 296. *Pons' Case.* (The account of this case is taken from the article on Retinitis Pigmentosa in the *American Encyclopedia of Ophthalmology*, Vol. xv., 1919.) Retinitis pigmentosa in three sisters, all of whom were blind from birth; the fundi were typical of the disease. In all three sisters both eyes showed a marked bulging of the cornea which had been noticed by the mother shortly after birth in each case; in other respects the sisters were normal and their health was good. Two sisters died in infancy of whom one was said to have been blind; a brother and a sister with normal vision died in adult age; two living brothers had good eyes. The parents were normal and unrelated, and there was no history of eye disease in the ancestry. There was no evidence of syphilis. No consanguinity. Bibl. No. 284.

Fig. 297. *Richter's Case.* Congenital night-blindness in three members of a sibship of nine, one sibling died in infancy. The parents and their ancestry were believed to be free from the defect. No consanguinity recorded. Bibl. No. 24.

Figs. 298 and 299 are described in our section on Glioma retinae.

SECTION V

CONGENITAL NIGHT-BLINDNESS

Plate XXIII. Fig. 300. *Sinclair's Case.* Fourteen cases of congenital stationary night-blindness in six generations. IV. 6, aged 50, and her son, V. 9, aged 11, were examined. For each case the ophthalmoscopic appearances were perfectly normal; V. = $\frac{5}{6}$ in each eye; fields for white were full in daylight, under diminished illumination it was found that a moderate reduction of light produced no change in the visual fields, but when the illumination fell below a certain point the fields became very markedly reduced as compared with those of a normal person; Förster's photometer, after twenty minutes adaptation, required the opening to be 7 as compared with 2 for a normal eye; colour vision was normal.

Of the affected members nine were males, five were females; all had normal vision and full fields in a good light but all were night-blind to such a degree that they were unable to go about alone after dusk. The night-blindness was in all cases congenital and non-progressive and was not associated with deafness or other hereditary defect. In 1907 the author informed Nettleship of the case in generation VI.; VI. 2—4 were still too young for examination. No consanguinity. Bibl. No. 235.

Fig. 301. *Sedan's Case.* Twenty-one cases of congenital stationary night-blindness in four generations, the affected individuals consisting of eleven males and ten females. An artillery officer in generation IV. was examined at the age of 30 when he had myopia of 3·5 D., colour vision normal, no definite contraction of visual fields and his fundi appeared to be perfectly normal; he had night-blindness which was not progressive and he stated that he had never been able to go about alone at night. The parents in generation I. appear to have been normal, both their daughters, four of their five grandchildren and ten of their nineteen great-grandchildren were affected. Ten years after the publication of this case Cutler (Bibl. No. 182) heard from the author that six more children had been born in generation V. of whom two were affected males; the exact parentage of these children was unknown. At a later date again Nettleship endeavoured to obtain further information of the family but was unsuccessful. No consanguinity recorded. Bibl. No. 136.

Fig 302. *Cutler's Case.* Congenital stationary night-blindness in three siblings of a sibship of thirteen. II. 3 was seen aged 42 (1881). On examination it was found V. R. = V. L. = $\frac{6}{24}$, or with weak concave glasses = $\frac{6}{18}$; he had a slight oscillating nystagmus; fundus was normal; central colour sense was normal; light sense = $\frac{1}{3\cdot5}$; there was a concentric narrowing of the fields for white. The other members of the sibship to be affected were II. 2, a male aged 44, and II. 5, a female aged 28. The three were married and had normal offspring. No further information was available and the family could not be traced. No consanguinity. Bibl. No. 182.

Fig. 303. *Fuchs' Case.* This case was first published by Nettleship to whom it was sent by the author. Two normal and unrelated parents, Benowicz by name, had three night-blind children. II. 1, a girl, aged 15, was first noticed to be night-blind at the age of 3; R. V. = L. V. = $\frac{6}{10}$ to $\frac{6}{15}$ with + 1·5 D. cyl.; light sense by Förster's photometer was $\frac{1}{20}$; fundi normal. II. 2, a girl, aged 11, was also first noticed to be night-blind when aged 3; R. V. = $\frac{6}{10}$, L. V. = $\frac{6}{20}$ not improved by glasses; light sense = $\frac{1}{25}$; fundi normal. II. 3, aged 8, a boy, was also night-blind and had normal fundi. No consanguinity. Bibl. No. 251, p. 409.

Fig. 304. *Hudson's Case.* Congenital stationary night-blindness in a mother and her two sons. II. 2 was seen aged 22; he had suffered from night-blindness as long as he could remember, he thinks the condition is improving, at any rate it is getting no worse; he was a dentist's mechanic and could see well in a good light but if the light failed in the least degree his vision was at once below the normal; fundus was quite normal; fields were about $\frac{1}{3}$ contracted; R. V. = $\frac{6}{18}$, with $\frac{-1\cdot0 \text{ sph.}}{-2\cdot5 \text{ cyl. axis } 165^\circ} = \frac{6}{9}$, L. V. = $\frac{6}{18}$, with − 2·5 D. cyl. axis 160° = $\frac{6}{9}$; there was an entire absence of any ophthalmoscopic signs pointing to retinitis pigmentosa. His mother and elder brother were the only two members of his family, so far as he knew, to be similarly affected. No consanguinity. Bibl. No. 224.

Fig. 305. *Stiévenart's Case.* Congenital night-blindness in ten members of four generations—both sexes being affected. I. 1, who lived to the age of 74, was night-blind; she had ten children of whom alternate individuals were born with this condition. One of her affected daughters, II. 2, who also lived to be 74, married and had three children, the first and third of whom were affected. Of these III. 1 had no children; III. 2 had very good sight and III. 3, a son, married twice, having one child, a son who was night-blind, by his first wife and by his second wife the first two children died in early infancy of diphtheria, the third child, a son, aged 4 years, was night-blind, and the fourth child, aged 2 years, had apparently normal eyes. Normal members of the sibship II. 2—11, who married, had normal offspring. The affected members could see perfectly well in the daytime or in a well lit room at night though they were a

little short-sighted. The eyes on examination presented nothing abnormal. No consanguinity recorded. Bibl. No. 30.

Fig. 306. *Cutler's Case.* Congenital stationary night-blindness in three sisters aged 42, 40 and 37 years respectively (1895). II. 5, a Russian Jewess, came up complaining of hyperaesthesia retinae; she was hypochondriacal and had been night-blind all her life; V. R. with + 1·5 D. cyl. = $\frac{5}{5}$, V. L. with − 5·5 D. sph. = ? $\frac{5}{6}$; light sense after adaptation = $\frac{1}{2\cdot5}$; fundus normal except for some narrowing of the retinal arteries. She had four children of whom one died in infancy and three are living and normal. In addition to her two night-blind sisters she had two normal sisters and three normal brothers; one sister had nine children and another had three children all of whom are normal (which sisters were married was unstated); one brother had seven normal children and another brother had three normal children by his first wife and six normal children by his second wife who was his cousin. The mother, I. 4, had cataract; the father, I. 3, had lost one eye from glaucoma; a paternal uncle, I. 2, became gradually blind and his daughter, II. 1, aged 15, was blind and was believed to have been born blind. Consanguinity. Bibl. No. 182.

Fig. 307. *Fuchs' Case.* This small pedigree of congenital night-blindness was sent by the author to Nettleship who first published it. II. 6, Rosa Bauger, aged 45, had stationary night-blindness; she was myopic, 7 to 8 D. and her corrected vision was $\frac{6}{18}$; her fields for white were decidedly contracted; the photometer showed very marked lowering of light-perception; the fundus was normal except for myopic changes and some opacities in the vitreous. She was the youngest in a sibship of five, the offspring of normal unrelated parents and she herself had four normal children. Her next elder sister, II. 5, was also night-blind, the other three siblings were normal but the eldest of these, a sister, II. 2, had one child who was night-blind. No consanguinity. Bibl. No. 251, p. 408.

Fig. 308. *Atwool's Case.* Congenital night-blindness in seven members of three generations, three males and four females being affected. III. 5 had never been able to see his way clearly at night; V. = $\frac{6}{6}$ in each eye; ophthalmoscopic appearances were normal. His father, II. 3, a naval officer, had more than once accidentally walked overboard from the bridge of his ship at night. A sister, III. 4, a hospital nurse, reported that she had been similarly affected as long as she could remember and was unable to go out alone in the dark; her refraction was hypermetropic, V. = $\frac{6}{6}$, fields and colour vision were normal and her fundi were dark but normal. Two brothers were normal, a sister, III. 1, was affected. Two paternal aunts, II. 1 and 2, and the paternal grandfather, I. 2, were also affected.

Nettleship made efforts to obtain further information of this family but had no success. No consanguinity recorded. Bibl. No. 180.

Fig. 309. *Langdon's Case.* Congenital stationary night-blindness without fundus changes in father and daughter. II. 1, aged 46 (1906), was given spectacles, and her R. V. with − 0·25 sph. − 1·50 cyl. ax. 100° = $\frac{6}{5}$, L. V. with + 0·25 sph. − 2·50 cyl. ax. 75° = $\frac{6}{5}$; the fundi were perfectly healthy. In 1909 R. V. with − 0·25 sph. − 2·25 cyl. ax. 100° = $\frac{6}{5}$, L. V. with − 3·25 cyl. ax. 75° = $\frac{6}{5}$. In 1910 she appeared again asking for her fields to be tested since she had all her life stumbled over objects and believed she had a scotoma; her fields were tested in a good light and found normal; her central light sense tested with de Wecker's charts = $\frac{4}{10}$ of normal for R. and $\frac{3}{10}$ of normal for L.

I. 1, father of II. 1, and a medical man, said that he had seemed to need a bright light to see even in boyhood; R. V. with + 1·5 D. sph. = $\frac{6}{5}$, L. V. with + 1·50 sph. + 0·25 cyl. ax. 120° = $\frac{6}{6}$; his fields were full in ordinary light; concentrically contracted in a dull light; no scotomata were present; fundi were normal; light sense by de Wecker's chart = $\frac{1}{2}$ of normal. His mother died at his birth and his father when he was aged 5, and no further family history could be obtained. No consanguinity recorded. Bibl. No. 304.

Fig. 310. *Fitzgerald's Case.* II. 1, a clergyman, aged 35 years, had been unable to see after sundown as long as he could remember; one of his three living sisters was also night-blind. His mother had fourteen children of whom two were still-born, seven died young of "water on the brain" and one son, II. 5, died aged 24 of probably tubercle. A distant cousin on the mother's side was also said to be night-blind. The patient, II. 1, had normal fundi, normal colour vision and slight myopia. No consanguinity. Bibl. No. 80.

Fig. 311. *Cant's Case.* (Published by Nettleship.) Night-blindness in two siblings, the offspring of first cousins. I. 1 had good sight, he died in middle age; I. 2 saw well. They had five children of whom II. 1, aged 24 (1908), was said by his mother to have been very short-sighted and night-blind since early childhood; he was examined by Nettleship and Usher and found to have myopia of about 10 D., retinal vessels were normal and fundus was normal except for moderate crescents; fields to rough hand test seemed full; his sight was conspicuously defective in a dim light. II. 2, aged 17, had myopia of about 3 D., she showed no shortness of sight till about the age of 13; she was not night-blind; fundus was normal. II. 3, aged 13, had been very short-sighted and night-blind since early childhood; she was found to have myopia of about 10 D., fundus was normal except for moderate crescents. The other two siblings were normal. Consanguinity. Bibl. No. 263, p. clviii.

Fig. 312. *Nettleship's Case.* II. 1, aged 60, suffered from night-blindness; her V., with + 1·5 correction, = $\frac{6}{18}$; fundus was normal except for a small patch of epithelial disturbance at the macula of the L. eye; there were striae in her lens. II. 2, aged about 50, had always had bad sight and suffered from night-

blindness; he could only see straight before him. II. 3 had ocular headaches but was not night-blind. No consanguinity recorded. Bibl. No. 251, p. 410.

Fig. 313. *Fuchs' Case.* (Published by Nettleship.) Two normal and unrelated parents named Wenzel had six children, II. 1—6, of whom the first four had normal eyes. II. 5, a labourer, aged 22, had always suffered from night-blindness; he was myopic −6 D.; corrected V. $= \frac{6}{12}$; fields for white were full; light sense by Förster's photometer $= \frac{1}{12}$; fundus was normal except for myopic changes. II. 6, a female, aged 19, was also night-blind but was said not to be myopic. No consanguinity. Bibl. No. 251, p. 409.

Fig. 314. *Bessonnet's Case.* Congenital stationary night-blindness in a mother and two sons. II. 1, aged 17 years, had suffered from night-blindness since an early age and was unable to go out alone in the evening; his parents could not remember that he had ever been any better than he was at the time of examination; his general health was excellent and he had normal vision in good daylight. Ophthalmoscopic examination revealed no abnormality; there were no scotomata and no contraction of visual fields. His mother and one of his brothers were similarly affected, in both cases there was nothing pathological to be found except night-blindness. No information is given of normal members of the family but the original account of the case was inaccessible and the above is taken from an abstract only. No consanguinity recorded. Bibl. No. 230.

Fig. 315. *Vieusse's Case.* II. 1, aged 40 years, reported that his parents had noticed at an early age that he became blind for two or three hours in the evenings, not even seeing large objects, and this condition had troubled him all his life. If he remained in a dull light all the day night-blindness did not develop in the evening; he had never noticed that fatigue affected the condition. In the day the pupils were very dilated and there was some contraction of fields but the fundal appearances were normal and there was no trace of pigment to be seen in the retina. A sister had the same symptoms as her brother but another brother, II. 2, had normal vision. The parents were first cousins with normal sight.

The patient was treated by protecting the eyes from bright light during the day either by means of tinted spectacles or by means of a dark veil.

The condition is not typical of congenital stationary night-blindness but it may be of some interest to include it here. Consanguinity. Bibl. No. 104.

Fig. 316. *Swanzy's Case.* II. 1, aged 27, was slightly amblyopic and had always been so, in the dusk his sight became very imperfect and as a child he had always needed to be led about as soon as twilight set in; the ophthalmoscopic appearances were normal; colour sense was normal; refraction was slightly hypermetropic. Of his siblings one brother and three sisters were also night-blind; the brother and one sister were abroad but the other two sisters were seen one of whom was emmetropic, the other slightly myopic; the night-blindness in the case of the two sisters who were seen was less severe than in the case of II. 1. The parents and ancestry were normal as far as was known. No consanguinity. Bibl. No. 83.

PLATE XXIV. Fig. 317. *Cunier, True and Nettleship's Case.* The pedigree of the Nougaret family of Vendémian showing a history of congenital stationary night-blindness was first published in 1838 by Cunier[1] who traced the defect through seven generations; seventy years later the history was brought up to date and considerably extended by Professor Truc and M. l'Abbé Capion, Curé of Vendémian, at the request of Nettleship who went over himself to examine certain of the cases and published the greatly enlarged pedigree extending now to ten generations in 1907[2]. A full history of the original discovery of the family and of the collection of facts is given in this paper where Nettleship also describes the nature of the country surrounding Vendémian and the conditions under which examination of individuals was carried out.

At the time of Cunier's work on the pedigree the ophthalmoscope had not been invented so that he was unable to definitely state the nature of the case and it was only in 1906 that Nettleship through Professor Truc was able to pronounce that the disease had been proved to be congenital stationary night-blindness, was not retinitis pigmentosa, and that further it was that type of congenital stationary night-blindness which affects and is transmitted by both sexes alike, is not characteristically associated with myopia and is never transmitted through a normal member of the stock.

Our efforts to hear whether any further cases of the defect have occurred in the family since Nettleship's publication have met with no success; the difficulty of the local patois and the tendency of the family to conceal the defect make it useless for anybody to try to obtain reliable information without the cooperation of workers living in the district.

Jean Nougaret, I. 1, a butcher, known as "le Provençal," born about 1637, is supposed to have introduced the defect into the parish of Vendémian; amongst his descendants the affected members now number 135 of whom 72 are male, 62 are female and one was of sex unknown; there appears to be some evidence to suggest that owing to concealment of the defect the real number of affected members may be even greater.

With regard to consanguinity, Nettleship noted forty cases of marriage within the stock, most of these cases occurred between distant cousins for the descendants of Jean Nougaret were Catholics and as such were forbidden to marry their first or second cousins without a special dispensation; many such marriages

[1] Bibl. No. 27. [2] Bibl. No. 243.

amongst normal branches of the family are not noted in the pedigree. V. 41, an affected male, married his second cousin, one of the females of V. 39; they had nine children of whom three were affected; VII. 63, an affected male, married VI. 121, his distant cousin, who was herself affected; this marriage resulted in two children both affected.

The cases examined by Nettleship were VII. 90, female, aged 46; VIII. 9, male, aged 51; VI. 76, female, aged 72, whose R. eye was nearly blind from glaucoma; VIII. 6, female, aged 55, her son IX. 8, aged 26 and granddaughter X. 3, aged 10 months; VII. 86, female, aged 58; VII. 100, male, aged 46 and his son VIII. 63, aged 16; VII. 115, female, aged 47 and her daughter VIII. 72, aged 21; VII. 63, aged 64, his wife VI. 121, aged 64 and three of his grandchildren IX. 27, 28 and 30, all of whom had normal fundi and were demonstrated to be night-blind; their refraction was mostly emmetropic or slightly hypermetropic; VII. 86 had myopia of 3 D., and they all had good vision in daylight. X. 3 was too young to test. In writing to Nettleship of the family the Curé said "the subjects of the night-blindness have no physical defects and see as well during the day as other people, indeed better according to their own statements, but on a moonless night they are completely blind; the adults learn to guide themselves at night in places with which they are familiar, and seem to recognise the presence of obstacles by some movement or displacement of the air, but unless the moon is up they cannot go beyond the village at night without either a guide or a lantern, and the night-blind children, not having learnt to compensate so well for the defect, have recourse to walking at night or in dark places with head erect, arms extended and hands open."

We should like to add here some tribute to the great contribution of labour and enthusiasm on the part of M. Chauvet, who originally drew up the pedigree for Cunier, and of M. l'Abbé Capion, the Curé, without whom it would have been impossible to obtain this record, who to quote Nettleship "devoted many hours of many days for nearly two years, with indefatigable patience, to the task of unravelling the complications of this genealogy." Consanguinity. Bibl. Nos. 27, 243.

Fig. 318. *Pagenstecher's Case.* Congenital stationary night-blindness affecting males only and transmitted by unaffected males or females. III. 3 brought his grandson, V. 1, to be examined, stating that the parents of the child had noticed lately that he was suffering from night-blindness. He himself, III. 3, suffered from the same condition as did one of his brothers, III. 5, all his four male cousins and his maternal grandfather, I. 1, who had told him that this condition had been inherited by the males of the family as far back as could be traced. I. 1 died in 1827, leaving a normal son, II. 2, and two normal daughters, II. 3 and 5. II. 2 married and had two night-blind sons; II. 3, the mother of III. 3, had two affected sons, one normal daughter and one normal son; II. 5 had two night-blind sons. In the next generation all were normal but IV. 2, the daughter of III. 3, had three sons, of whom one was night-blind. III. 3 was examined and found to have myopia of 3 to 4 D.; there was some opacity in the L. lens; ophthalmoscopic appearances were normal; on lowering the light his vision became rapidly reduced and there was a concentric contraction of his fields; colour vision was normal. V. 1 was night-blind and ophthalmoscopic appearances were normal; his mother, IV. 2, was examined, but no trace of night-blindness was found. V. 2 and 3 were probably too young to be examined and Nettleship was unsuccessful in his efforts, at a later date, to obtain further information. No consanguinity recorded. Bibl. No. 102.

Fig. 319. *Nettleship's Case.* Five cases of night-blindness from infancy or birth, limited to males and transmitted through unaffected females, associated with myopia. I. 1 and 2 had good vision, I. 2 was "mad" for some weeks before his death at the age of 77. They had eleven children of whom five died young, the two living sons, II. 1 and 6, had been night-blind all their lives and were not getting worse; II. 1, aged 40, wore glasses in the street and was probably myopic; II. 6, aged 28, did not wear glasses. Of the daughters II. 2 had two children with normal vision whose sex was not recorded; II. 4 had two sons of whom III. 3 was very night-blind and died of diphtheria aged 2 years; III. 4, aged 7 years, saw quite well at night. II. 7 had three sons one of whom, III. 5, aged 5, was noticed by his mother to be night-blind at the age of 12 months, his pupils were normal in their reaction to light but were rather large; refraction, myopia 4 D., moderate crescents were present; vessels were normal; there was an appearance of coarsening of the pigment epithelium in some parts but nothing incompatible with health; colour vision normal. His brother III. 6, aged 3, was night-blind and myopic; he had small crescents and a single minute dot of black pigment in the left upper periphery; he had large pupils and a fine lateral nystagmus. III. 7, aged 12 months, and III. 8, aged 3 years, were reported to have normal vision. No consanguinity. Bibl. No. 251, pp. 418—9.

Fig. 320. *Nettleship's Case.* This very extensive pedigree of congenital stationary night-blindness consists of two pedigrees previously published and believed to be unrelated, one by Stanford Morton[1] in 1893, the other by Nettleship[2] in 1908; the relationship was discovered and the combined pedigree was published in its completed form[3] in 1912.

The night-blindness here is of the type which is confined to the male sex and transmitted through the unaffected females and as is usual in this type is associated with a high degree of myopia and with a considerable amount of defective visual acuity, there is also associated in this case a prevalence of mental

[1] Bibl. No. 175. [2] Bibl. No. 251, pp. 419—21. [3] Bibl. No. 282.

instability. The degree of night-blindness was stationary in all cases, present from earliest recollection and was accompanied by no fundus changes other than those due to the myopia.

IV. 4 and IV. 8 are the earliest cases definitely known, but it was asserted by some relatives and denied by others that the grandfather of these brothers, probably II. 3, was also night-blind. IV. 4 died aged 42 of kidney disease, he was believed by VI. 10 and VI. 51 to be short-sighted. No information as to myopia in IV. 8.

Generation V. was free from night-blindness but two members, V. 9 and V. 17, were myopic and there was a fairly heavy infant mortality.

Of the sibship VI. 5—11 four out of six males were night-blind and myopic from the earliest recollection; this family was in Australia and information was given by VI. 10, a solicitor, whose reading glasses were—R. – 8 D. sph., – 4 D. cyl.; L. – 4 D. sph., – 5 D. cyl.; axes nearly vertical; his sight was good when corrected. There is no measure of the refraction of VI. 5, 7 and 9. VI. 5, 6, 7 and 8 are married and have normal children of both sexes, one or two of whom are said to be slightly short-sighted. VI. 9 died young of rheumatic fever; VI. 10 is unmarried. Of the sibship VI. 12—23, VI. 20 died in infancy and three of the remaining six males are night-blind and myopic; and two males, VI. 17 and 19, who are not night-blind, are said to be "near-sighted," two females also, VI. 12 and 22, are said to be near-sighted. There is no measure of the refraction in this sibship. VI. 15, 17 and 23 have normal children. Of the sibship VI. 25—35 two out of three males were night-blind and myopic, one of them, VI. 31, being also mentally defective, three died in infancy, VI. 28—30, and one female, VI. 32, was night-blind to a less degree than her brothers but was not myopic. This is the only female in this pedigree to be affected and it was only after most careful investigation that Nettleship classed her as an undoubted case of the disease. She was aged 48, had a slight astigmatism and with a correction for this saw $\frac{6}{6}$ with each eye; her light perception appeared to be normal yet she had some difficulty in going about alone on a dark night, but it was chiefly on the basis of the perimetric results that Nettleship decided upon his diagnosis. VI. 31 was night-blind to a less degree than his brother VI. 35, he used – 5 D. spectacles from about the age of 17 till his death from intestinal obstruction at the age of 41; he had been in an asylum and was mentally defective. VI. 35 was under observation for a considerable period of years and his refraction was measured from time to time. At the age of 14 he had – 5 D. spectacles probably for distance, at the age of 21 his myopia was about 10 D. and increased to 13 D. by the age of 35; when last examined by Nettleship at the age of 41 (1911) there had been no further increase. The light sense with Förster's photometer after 20 minutes adaptation was about $\frac{1}{10}$th compared with Nettleship's; his fields were taken under varying conditions and are given in the original paper; he has always been very blind at night and for the rest he is a healthy vigorous farmer with dark brown irides and hair. There is no information of children from any members of this sibship.

The sibship VI. 36—47, the offspring of an unaffected daughter of IV. 4, have all perfect sight (VI. 36 died in infancy and so condition of sight was unknown), VI. 45 is believed to have died from suicide and VI. 46 was reported to be in an asylum. V. 17 married his first cousin and had ten children, VI. 51—65, of whom four died in infancy and the three males who survived were all night-blind and myopic; one female, however, VI. 53, who married and had seven children, did not transmit the disease. VI. 51 was a nervous type of individual, he was wearing – 4·5 sph. – 2·5 cyl., axis nearly vertical for each eye, and this appeared to exactly correct his refraction over an extensive period of years; V. = $\frac{6}{12}$ nearly; light sense with Förster's photometer was $\frac{1}{16}$ (no note of adaptation time); has been night-blind all his life. VI. 55 was night-blind and short-sighted and his eyes were said to be "not straight"; he lives abroad and no further particulars could be obtained. VI. 59 had been night-blind all his life; he had had both external recti cut at the age of 19 and the L. eye was still somewhat divergent; at the age of 34 Nettleship found R. – 6 sph. – 2 cyl. V. = $\frac{6}{9}$; L. (divergent) – 6 cyl. – 5 cyl. V. = $\frac{6}{24}$; colour vision apparently normal; the R. fundus showed three or four small round dots of pigment but the O. D.'s and vessels were normal and there was nothing to suggest retinitis pigmentosa. VI. 48—50 were three normal offspring of V. 17 by a second unrelated wife. VI. 66—68 are three brothers of whom 66 and 67 died young and were epileptic and imbecile and 68 had a history of repeated pulmonary haemorrhages, he had excellent sight. Of the sibship VI. 69—74, VI. 71 is short-sighted, considers that he sees less well than other people at night and Nettleship had little doubt that he was night-blind in some degree though his relatives did not consider him to be so. VI. 74, a female, is said to be mentally very peculiar. The only remaining case of night-blindness in this generation is VI. 82, aged 50 (1911). He began to wear glasses at the age of 9 years; at the age of about 17 he was ordered – 8 D. and after this his refraction was observed from time to time and had increased little if at all when Nettleship finally examined him at the age of 50; at this time with correction R. V. – L. V. = $\frac{6}{12}$ part; colour sense was normal; fundus normal; choroids decidedly light; light sense after 20 minutes adaptation $\frac{1}{16}$ (compared with Nettleship's); fields were examined under a variety of conditions and are given in the original paper; he had been suspected of phthisis but developed into a hard-working rector with excellent health.

In generation VII. there are four affected individuals. VII. 45 and 46 the only two males in their sibship are both night-blind and highly myopic. VII. 46 also is said to be a little mentally deficient and to have nystagmus; the pupils of both brothers are said to be habitually large; the spectacles of VII. 45

are said to be about – 9 to – 12 D. The four sisters were intelligent and had excellent vision. VII. 49, aged 30 (1911), has been under observation since he was seen by Stanford Morton at the age of 12. He had fair vision then with his myopia corrected and perfect colour vision; night-blindness, with no visible fundus change, from earliest recollection, and concentrically contracted fields. Nettleship examined his refraction at the age of 13 and found for R. – 2·5 sph. – 2 to 3 cyl., V. = $\frac{6}{18}$ – $\frac{6}{9}$; L. – 2 sph. – 2 cyl., V. = $\frac{6}{18}$ – $\frac{6}{9}$ which was practically the same when examined again at the age of 30. Irides blue or blue-grey; light sense by Forster's photometer furnished with a plain sheet of white paper at the end, after 20 minutes adaptation nearly $\frac{1}{5}$ (compared with Nettleship's); fields were taken under varying conditions and can be seen in the original; there was a crescentric relative scotoma enclosing the blind spot. The other members of his sibship have normal sight.

VII. 56, the only child of VI. 85, writes from America that he wears spectacles constantly and that he cannot see after dusk, he sends the prescription for his spectacles showing them to be – 9 D. sph. For any further information about the members of this pedigree we must refer the reader to the original article. Consanguinity. Bibl. No. 282.

Fig. 321. *Newman's Case.* An interesting pedigree of congenital stationary night-blindness in males only transmitted through unaffected females only and associated with myopia and pterygium. I. 1, Joel Bryan, was a quaker in North Carolina, probably of English extraction; the condition of his eyes is unknown but his cousin, I. 3, a physician named Thomas Vause, is known to have been night-blind. II. 1, Margaret Uzzell, daughter of I. 1, had normal vision but transmitted the defect to three of her four sons; she had also five normal daughters. II. 2 was normal.

III. 1 was night-blind; III. 2 was believed to be normal and to have normal offspring. III. 4 and 6 were normal and had normal offspring. III. 8, aged 74 (1912), had been night-blind since infancy, he was also "short-sighted" and suffered considerably from pterygium; all his children were normal with regard to night-blindness but many of his grandchildren were affected. III. 9 was normal. III. 10, aged about 70 (1912), was night-blind, myopic and had a pterygium; he also had normal children but affected grandchildren. III. 11 had normal vision. III. 12 and her progeny were believed to be normal. III. 14 and her progeny had normal vision. III. 16, the only normal son of II. 1, had normal descendants.

In generation IV., of the children of III. 8, none were night-blind but six out of ten (4 males and 2 females) suffered from pterygium; members of other sibships of this generation were all normal.

In generation V., of the seven children of IV. 6 who suffered from pterygium, all were normal with regard to night-blindness but three males suffered from pterygium, two males and two females were normal, one of the females died in infancy. V. 8—14 consists of five normal females and two night-blind males, one of whom V. 14 had strabismus; V. 9 was reported to be night-blind and to have the associated defects; their mother, IV. 8, Mrs Brown, had pterygium but none of her children had this affection. Of the sibship V. 15—21, the offspring of the normal IV. 10 (Mrs Hobdy), five out of seven males were night-blind and three of these were also myopic and had strabismus. V. 22, the only son of IV. 12 who suffered from pterygium, was normal. V. 23—26 consists of two normal females and two night-blind males, one of whom was also myopic and had strabismus; their mother, IV. 14, Mrs Floyd, suffered from pterygium. V. 27—30 consists of two normal females and two night-blind males; their mother, IV. 18, Mrs Hurst, was normal. V. 33—36 consists of one normal male, V. 33, two night-blind and myopic males, V. 34 and 35, and one normal female, V. 36; their name was Montgomery. The only other affected member of this generation is V. 39, the only son of IV. 30, who was night-blind; his name and age were unknown. No consanguinity. Bibl. No. 300.

Fig. 322. *Cant's Case.* (Published by Nettleship.) Night-blindness without visible changes in the fundus in three myopic males. I. 1 lived to be 90, she became blind in her old age; her daughter, II. 2, had three children, of whom III. 2 was reported by his daughter to have been very short-sighted and night-blind all his life and had always had to be led about after dusk, he could see quite well in the day, he died aged 76; III. 4 and III. 6 had perfect vision throughout life. III. 2 married twice, by his first wife he had a daughter, IV. 2, by his second wife he had three sons and two daughters all with good sight. IV. 2 had an illegitimate son, V. 1, who was examined by Usher and Nettleship; he had been short-sighted and unable to see at night as long as he could remember; he had myopia of 7 D. in R. and 10 D. in L. at posterior pole with decidedly less at the periphery; his fundus was normal except for moderate myopic crescents; marked night-blindness was demonstrated; he had one child, VI. 1, aged 8, with perfect sight, normal fundus and no night-blindness, she had hm. of 2 D.

IV. 5, daughter of III. 2 by his second wife, had two children, a daughter aged about 20 with normal vision and a son, V. 5, who was night-blind and myopic. V. 5 had been given – 6 D. spectacles by Cant in 1889 when he was aged about 5 and was seen at intervals after this; at the age of 14 R. V. with – 10 D. = $\frac{6}{12}$, L. V. with – 9 D. sph. – 1·5 D. cyl. = $\frac{6}{9}$ partly; he was seen by Usher and Nettleship who demonstrated his night-blindness and noted his normal fundi.

V. 10, a grandson of III. 4, was reported to have been very short-sighted and the mother of V. 5 wrote that "she thought he was afflicted in much the same way as her son"; he died aged 25; he had about six siblings who all saw well. V. 12, a granddaughter of III. 6, was said never to have had good sight and eventually went blind, she was dead and no particulars were known.

IV. 5 and 6 had perfect vision. The parents of V. 5 were known to be unrelated. No consanguinity recorded. Bibl. No. 263, pp. clv—clviii.

Fig. 323. *Nettleship's Case.* Twenty-two males affected with congenital stationary night-blindness in three generations, the only four cases examined were also myopic. I. 1 and 2 were normal and unrelated; they had thirteen children of whom six were females with normal vision, five were of unknown sex, and two sons, II. 6 and 16, were reported to have been night-blind. II. 6 married and had two normal sons, four normal daughters; II. 16 had one normal son, two night-blind sons and two normal daughters. Of the unaffected daughters of I. 1 and 2, the eldest had one normal child, a son; II. 3 had two night-blind sons, one of whom was married and had a normal son; II. 8 had two unaffected daughters, III. 9 and 12, two night-blind sons, one of whom was married and had a normal son, and one unaffected son, III. 15. II. 10 had one unaffected son, three unaffected daughters and four night-blind sons, of whom one was married and had six normal daughters and two night-blind sons; another, III. 19, was examined by the author, he was myopic and had a normal fundus.

II. 13 had three night-blind sons, III. 23—25, and four normal daughters; one of the daughters was married and had one night-blind son and one normal son. III. 24, aged 26, was intelligent; he had a quick lateral nystagmus when looking sideways; colour sense was normal; he had always seen badly at night; with − 11 D. R. V. = $\frac{6}{18}$, L. V. = $\frac{6}{36}$; the fundus showed no definite changes except myopic crescents and perhaps some pallor of the discs. III. 25 had high myopia and saw worse at night; his fundus showed no definite changes; he was very excitable, liable to fits and at times became demented.

II. 14 had one normal son, two night-blind sons and four normal daughters.

III. 9 had two normal daughters and two night-blind sons, IV. 3 and 4. IV. 3 was examined three times during a period of several years and the condition was not quite typical in his case; he was intelligent and healthy but saw so badly at night that he was unable to go about alone even in the house; his colour vision was normal; he had myopia of 4·5 D.; the choroid at the central regions was granular and pale as if from disease of the epithelium, also there were some scattered pigment spots of uncertain significance; neither the fundus condition nor the myopia progressed or changed in any way between the ages of 5 to 10 years during which he was under observation. III. 12 had two normal sons, IV. 7 and 8.

The defect in this family was confined to males and was transmitted by affected males and also by unaffected females. No consanguinity recorded. Bibl. Nos. 151, 251, p. 422.

Fig. 324. *Nettleship's Case.* II. 2, seen aged 51, had congenital stationary night-blindness; V. = $\frac{6}{9}$ with and without + 0·5 D. cyl.; his fundi were quite normal except at the lower periphery where he had on the right side one or two small patches of choroidal atrophy and on the left side a good deal of superficial disturbance of the choroid. No signs of hereditary syphilis. He was the eldest son of a father who was affected in the same way and who never became blind. Of his seven children III. 1, a daughter, was normal; III. 2, a night-blind son, had one child aged 2 years; III. 3 represents three living normal members (sex not given); III. 4 represents two children who died. The author was unable to obtain further information. No consanguinity recorded. Bibl. No. 251, pp. 404—6.

Fig. 325. *Cutler's Case.* I. 1, a mason by trade and a very strong and healthy man, who lived to be 80 years of age, suffered from night-blindness all his life; the condition was stationary and in a good light his vision was excellent; nothing was known of his ancestors. II. 2, the only child of I. 1, had good sight, as also had her husband; of her three sons two suffered from night-blindness, and of her four daughters one died in infancy and the other three transmitted the disease. Of the affected sons III. 5 died aged 9 years but had previously been examined by Professor Arlt; III. 8, a mason, was seen aged 46; he was an intelligent man with good health but had always suffered from night-blindness which was stationary; pupils were normal, media clear; the R. fundus was somewhat tessellated, the retinal pigment being uniformly rather scanty but not to a pathological degree; the vessels were perhaps a little narrow; there was no change since he was examined three years previously; colour vision was normal; R. V. = $\frac{6}{12}$ not improved by glasses, L. V. = $\frac{4}{60}$; light sense with Forster's photometer was $\frac{1}{19}$ (minimum opening of 14 mm. compared to 2 mm. for a normal person) with slight improvement after adaptation for 15 minutes; the lower temporal arteries were noted as being rather small relatively to the upper ones. III. 2, who died aged 22 years, was normal. III. 3, who was normal, had four sons, of whom IV. 1, aged 28 years, had myopia of 9 D. but no night-blindness; light sense normal; corrected vision = $\frac{6}{18}$; fundus had some spots of choroiditis. IV. 2 died aged 6; IV. 3 died aged 1 year; IV. 4, aged 21, had always been night-blind and near-sighted. R. V. = finger counting, with − 9 D. = $\frac{6}{24}$, L. V. = $\frac{6}{60}$, with − 9 D. = $\frac{6}{24}$; he had a quick lateral nystagmus; pupils normal; central colour sense normal; light sense defective; fundus as in the case of his uncle III. 8. III. 6, herself normal, had two daughters who died in infancy, one son, IV. 5, who died aged 7 years and was believed to be normal and one son, IV. 6, aged 13, who was night-blind and had myopia of 2 D.; his light sense was $\frac{1}{36}$ after adaptation; corrected vision was $\frac{6}{18}$; fundus was normal except for a crescent and an oval disc. III. 8 had two sons and three daughters, all of whom were normal. III. 10 had two normal daughters and one son, IV. 12, aged 18, who was night-blind and slightly hypermetropic; V. = $\frac{6}{12}$ to $\frac{6}{18}$; central colour sense normal; light sense $\frac{1}{25}$ after adaptation; fundus normal. No consanguinity. Bibl. No. 182.

PLATE XXV. Fig. 326. *Pflüger's Case.* Seventeen cases of congenital stationary night-blindness in males only, invariably associated with myopia and nystagmus, and transmitted through unaffected females in four generations; in one woman, IV. 4, and four men, IV. 28, 30, V. 10 and 22, myopia was noted without night-blindness. Only two of the cases were examined; a male, aged 40, in generation IV. had myopia 6 D., corrected V. $= \frac{6}{18}$, R. convergent strabismus, varying rotatory nystagmus, colour sense normal, light sense much lowered, fundus normal except for a crescent down out equal in size to O. D. A child aged 3, in generation V., was examined but notes of the case were missing; he had nystagmus and very severe night-blindness with no decided ophthalmoscopic changes. No consanguinity. Bibl. No. 124.

Fig. 327. *Nettleship's Case.* Two cases of congenital stationary night-blindness associated with myopia in brothers; the family history was fully worked out for five generations, a considerable amount of myopia was reported in other members of the stock but no further cases of night-blindness. The parents of the affected sibship were first cousins.

IV. 2, aged 47 (1900), had been night-blind all his life; he was myopic and began to use glasses at about the age of 12, he had – 7 D. since the age of 25 but now had myopia of 9 D.; V. $= \frac{6}{9}$; fields were full in daylight but there was a slight concentric contraction in very dull artificial light after 15 minutes adaptation; photometer after 5 minutes adaptation showed light sense of $\frac{1}{50}$; colour vision good; teeth good, no signs of hereditary syphilis; fundi were perfectly normal except for myopic crescents; the night-blindness was not getting worse. The elder brother of IV. 2 was also night-blind and the younger brother, IV. 4, who died aged 39 and had very good vision, used to lead his affected brothers at night when they were boys; their two sisters, IV. 5 and 7, were not night-blind but IV. 5 was slightly short-sighted.

Short-sight was noted in the father, III. 3, and two of his brothers, also in his mother, II. 4, and in four other members of the stock, III. 10, IV. 14, 16 and 17. Consanguinity. Bibl. No. 251, p. 421.

Fig. 328. *Fuchs' Case.* (Published by Nettleship.) Night-blindness in three brothers associated with myopia in at least one of them. II. 1, aged 39, had well-marked night-blindness which had been noticed in very early childhood; refraction, myopia – 4·5 D. for right, – 3·5 D. for left, corrected V. $= \frac{6}{24}$; fields for white were full in a good light, a little contracted in a dim light; fundus normal. His two brothers were said to have the same defect but no statement is made as to their refraction. No mention is made of any normal members of the sibship. The parents had good vision; they were distantly related. Consanguinity. Bibl. 251, p. 416.

Fig. 329. *Förster's Case.* Congenital night-blindness in two brothers. II. 1 was seen aged 14 years, he had perfectly good sight in daylight but in the evening or a dull light needed to be led about by a guide; his fundus was normal and his visual fields full in a good light and only slightly contracted in a dull light. His brother, II. 2, was similarly affected whilst his other siblings and his parents had normal sight. No consanguinity recorded. Bibl. No. 37.

Fig. 330. *Donders and Maes' Case.* Congenital stationary night-blindness in a father and three of his sons; two younger sons and one daughter had normal sight. III. 1 was examined by Donders in 1854 when he was aged 16, he suffered from very pronounced night-blindness. III. 3 was examined by Maes in 1861 when he was aged 19; his vision was good in daylight and ophthalmoscopic appearances were normal; his night-blindness was less severe than that of his brothers. The parents were related "in the sixth degree." The father, II. 3, aged 58 in 1861, had suffered from stationary night-blindness since his youth. Consanguinity. Bibl. Nos. 33, 43.

Fig. 331. *Maes' Case.* Congenital stationary night-blindness in three brothers whose six sisters had normal vision; the parents and grandparents were normal and unrelated; several children of a maternal aunt were also said to be affected with the same disease but their mother had normal vision. One case only was examined, he a schoolmaster, had myopia of $\frac{1}{10}$, was night-blind and had a slight bilateral rotatory nystagmus. Ophthalmoscopically he showed signs of a commencing atrophy of the choroid and retina, there were no perceptible changes at the yellow spot. No consanguinity. Bibl. No. 43.

Fig. 332. *Ammann's Case.* Congenital night-blindness in five generations of the type that is confined to males and transmitted only through the unaffected females. Information of the family was scanty, for one case only, VI. 3, was examined; he had myopia of 9 D. and said that all the night-blind members of his family were also short-sighted and that all who saw well at night had ordinary sight. The family ancestor, Andreas Steiner, 1750—1838, I. 1, had good sight; nothing was known of his or his wife's ancestry; he had two night-blind sons and one normal daughter who transmitted the defect to all her three sons, and of her two normal daughters one who married transmitted the defect to two of her four sons; the children of the night-blind son, II. 2, were all normal but the two daughters who married transmitted the defect in the one case to an only son and in the other case to one out of four sons, the other three being normal. In generation V. there were four individuals affected and two normal males in an affected sibship. In generation VI. there was only one night-blind male, VI. 3, who was examined by the author; he had two normal brothers. The pedigree as here given is taken from an extension, with slight alteration, of the original pedigree as communicated by the author to Nettleship (see Bibl. No. 251, p. 415). No consanguinity recorded. Bibl. No. 197.

SECTION VI

GLIOMA RETINAE

(a) GENERAL ACCOUNT

Only a very brief account will be given here of the chief characteristics of glioma retinae; the subject is of great importance to the clinician but has been of no very great interest from the point of view of the student of heredity, because inherited cases are extremely rare and such family histories of the condition as exist are scanty and only in a few cases does knowledge extend beyond the single sibship with its parentage. Until recent times the condition was almost invariably fatal at a very early age and no family with a liability to the disease would be at all likely to survive; with the multiplication of hospitals and clinics, the great advance in surgical technique and the increased skill and knowledge which lead to an earlier diagnosis the fatality has become markedly reduced until now we know that provided the child is operated on early enough recovery may be expected. It is true that survival for the victims of glioma retinae inevitably involves the loss of one or both eyes but this deformity is not invariably a bar to marriage as we see from Figs. 333, 336—338, 340—343, 345 and 361 of Plate XXVI; indeed so active to-day is the instinct to protect those who have a serious handicap in life that marriage may come rather readily to these victims, and in every one of these cases in which an affected member survived and married the disease has reappeared in the next generation. It is possible of course that these cases were published because the affected offspring occurred and so the family came again into the hands of the medical profession; it would be of great interest to hear of cases in which affected members who have survived and married have had only normal offspring. Further, glioma retinae in an individual is to-day regarded as no bar to the marriage of his unaffected siblings or of other more remotely related members of his stock and yet a glance at Figs. 334, 335, 339, 342, 344 and 366 is enough to raise grave doubts as to whether any member of a sibship in which more than one member is affected ought to marry; added to this the observation that in certain sibships the disease is of such remarkable dominance, as for example in Fig. 349, where all the eight children of a sibship were affected, or in Fig. 339, where ten children of a sibship of sixteen died from the disease and two of the remaining six siblings died in infancy from other causes, brought before us the necessity for a review of all available material if we would avoid the occurrence of suffering in the next generation as a result of the application of the increased skill and knowledge in this. Accordingly we decided to search through the literature and collect for this volume all cases recorded in which more than one case had occurred in the same stock. The disease is rare and, on the basis of frequencies given by Wintersteiner, Adam, Vetsch, Plant, von Graefe, Trantas, Caspar, Stieren, Lowtzow and Alvarado, probably accounts for not

more than ·03 °/₀ of all patients suffering from disease of the eyes, so that multiple cases in the same family become of great significance.

Glioma retinae is a new growth of the retina which occurs exclusively in very young children and is malignant in that it infiltrates surrounding structures, may extend by proliferation of the primary growth, by continuity along the optic nerve to the brain or may be widely disseminated by means of the lymph channels or blood stream forming metastases in the glands, bones or occasionally distant organs of the body. The condition has been variously described in the literature of the subject under the title of *fungus medullaris oculi*, *fungus haematodes*, encephaloid degeneration of the retina, *carcinoma oculi*, *cancer atrophicus oculi*, *medullary sarcoma retinae*, glio-sarcoma, neuro-epithelioma and neurocytoma, names which collectively suggest many of the fundamental characteristics of the tumour which is of rapid growth, may be extremely haemorrhagic and of a soft or spongy consistency; superficially the microscopic appearance of the tumour resembles that of a small round-celled sarcoma but on close examination of a fresh specimen the cells of glioma retinae are discovered to be peculiar to it and to differ from those of sarcoma, they possess large nuclei and relatively very little cytoplasm which in a fresh specimen appears to be drawn out to form long thin interlacing processes or fibrils; the cells tend to occur in ring-like formation, typical of the condition, which have come to be known as 'rosettes'; the name of glioma retinae was given to this growth by Virchow[1] from the belief that it originated in the connective tissue of the retina and was therefore comparable in nature to the cerebral glioma which originates in the neuroglia of the brain, but Treacher Collins[2] has pointed out that the tumour is composed of cells which resemble those of which the whole retina is composed in the third month of foetal life before the differentiation of its layers, and it has been suggested that neurocytoma or neuro-epithelioma is the more applicable name for the condition which is possibly due to misplacement of retinal cells during foetal life, these cells retaining their primitive character and subsequently multiplying to form a parasitic growth.

We should like to quote from the description of a case by Hayes[3] in 1767 as illustrating the entire lack of recognition of the condition at that time by even so close an observer as John Hunter: the patient was a child aged 3 years who was brought to Hayes with an affection of both eyes in 1764, some defect having been first noticed by the parents in the left eye when the child was aged 15 months; Hayes was puzzled by the case and consulted with John Hunter and other surgeons—he says "None of them however pretended to understand the case..."; a foreigner who had obtained great reputation as an oculist was then consulted, "he giving the most confident assurances of restoring the right eye and even some hopes of retrieving the other, she was put under his care. He said it was a liquefaction of the crystalline humour, a case he had often met with, but after two months' strict perseverance in a very whimsical course of medicine the patient grew much worse...." Hayes then operated in the presence of John Hunter, he "passed a needle as for cataract operation thinking the condition was due to an excess of secretion," but then the true position became evident and

[1] Bibl. No. 13. [2] Bibl. No. 46. [3] Bibl. No. 3.

Hunter removed the eye. The child died a few months later and the *post-mortem* examination is described. This case is of rather special interest from its association with John Hunter, it is not however the earliest case which may be identified as belonging to our subject; Paw[1] for example describes a case, with subsequent *post-mortem* examination, of a tumour the size of two fists protruding from the left eye of a boy aged 3 years seen in 1597.

In 1809 Wardrop[2] discusses 17 cases of glioma retinae which he has collected, he describes the external appearances and the appearance on dissection and distinguishes between this condition and cancer[3]; he notes that in every case, which he has seen or heard of, all treatment including extirpation had been unavailing except a doubtful instance in a woman aged 58 (and we know now that this was certainly not glioma retinae) which had not recurred after 10 months. He adds that in no case had the eye been extirpated in the very early stages—a very significant and important observation as we now know; for if the course of the disease may be regarded as passing through three stages—Stage I in which the eye is blinded and a whitish or golden yellow reflex is seen in the pupil[4] due to the growth behind the lens, Stage II in which the intra-ocular tension is raised and the eye becomes painful, Stage III in which the growth spreads along the optic nerve or through the cornea—the probability of cure appears to be almost entirely dependent upon the stage at which operation is performed, as is well illustrated by Adam's[5] analysis of 43 cases treated by him as follows:

Stage of disease	No. treated	No. cured	No. in whom there was recurrence
I	5	5 = 100 %	0
II	14	12 = 85·7 %	2 = 14·3 %
III	16	1 = 6·3 %	15 = 93·7 %
?	8	6 = 75 %	2 = 25 %

Much has been written on the subject of glioma retinae, frequent reference is made to the fact that multiple cases are known to occur in the same family and several extremely valuable attempts have been made to collect all the available material on the subject and to give statistical information as to the sexual incidence, age of onset, distribution of metastases when they occur, cure and recurrence of the disease and bilateral or unilateral nature of the disease; we would specially refer to the works of the following writers—Hirschberg[6], Vetsch[7], Lawford and Collins[8], Marshall[9], Wintersteiner[10], Adam[11], and Berrisford[12]; these authors consider the disease as a whole, paying no special attention to the hereditary cases.

[1] Bibl. No. 1. [2] Bibl. No. 5.

[3] Hey, writing to the editors of the *Medical and Physical Journal* in 1804, says that fungus haematodes is described as a spurious aneurysm by one surgeon and that another gentleman considers it a species of cancer but that both are wrong.

[4] An appearance described by Beer as 'amaurotic cat's eye.' [5] Bibl. No. 44.

[6] Bibl. Nos. 17, 18 [7] Bibl. No. 24. [8] Bibl. No. 27. [9] Bibl. No. 30.

[10] Bibl. No. 31. [11] Bibl. No 44. [12] Bibl. No. 50.

We have been able to collect 36 small family histories of glioma retinae from the literature giving records of 128 cases, each of which belongs to a stock in which one or more further cases of the disease occurred; the history is in many cases extremely scanty, the sex of the individual not being given nor his age at the time of onset, nor whether or no he had normal siblings; we have however from the severity of the condition the assurance that the diagnosis is in all cases almost certainly a correct one and that cases are very unlikely to have been screened.

The age of onset of glioma retinae is very indefinite so far as actual age in years or months is concerned; we are frequently told the age at which the parents first noticed that all was not well with the child, but observation of their children's welfare differs greatly from parent to parent; in other cases we are only told the age at which the child was first taken to the doctor, which again gives little indication of the age of onset of the disease or the length of time during which it has been progressing; several authors[1] have given age frequency distributions but we feel that all that we can insist upon is that the disease is one of infancy or early childhood, that it may already be present at birth and that only very rarely does a case occur later than the age of 7 years.

On looking through our histories for evidence of associated disease in the affected or unaffected members of our stocks, we find no significant relationships and repeatedly the affected child is described as being healthy and well-developed in all other respects; there is no evidence suggesting that other forms of malignant disease tend to occur in these stocks, a mother of affected members may be seen to have died from cancer of the breast in Fig. 335, Fig. 360 shows a father who died from cancer of the stomach, Fig. 366 a father who died from sarcoma of the thorax, but considering the great prevalence of malignant disease in the general population we cannot feel that these cases have any special significance; the case of coloboma of the choroid and iris in Fig. 363 in the normal sibling where two brothers had glioma retinae is suggestive but other pedigrees give no support to the theory that other congenital defects or anomalies might reasonably be looked for in association with glioma retinae. The stillborn babies of Figs. 343 and 345 are again suggestive, but on examination we can find no evidence of any specially high rates of stillbirth or of infant mortality in the recorded families.

With regard to consanguinity in parentage and its effect upon the production of glioma retinae we have no knowledge, in only two of the families has any statement on the subject been made and in neither case was consanguinity present; we are thus unable to make any statement as to whether consanguinity in parentage is a significant factor in the etiology of glioma retinae.

Our material again is too scanty to allow us to make any statistical statements concerning the sex incidence of the disease, the frequency and relative mortality of its bilateral or unilateral nature and the proportions of affected and unaffected in the sibship. We have in actual numbers an excess of males affected, but we cannot insist

[1] For example see Adam, Bibl. No. 44. Vetsch, Bibl. No. 24. Berrisford, Bibl. No. 50.

upon this excess on the basis of so small a sample; further we have a considerably higher proportion of bilateral affections in our hereditary cases than is given by Berrisford for his presumably chiefly isolated cases; but again this point is very indefinite for though the bilateral cases may be regarded as positive information the unilateral reports merely indicate that bilateral affection had not occurred, and in some cases all that this can be taken to mean is that when death intervened no affection of the second eye had yet appeared; we should need far more information and a consideration of the death-rates in the two groups before we could insist upon an excess of bilateral affections in hereditary cases.

It is hoped that the few pedigrees we have been able to collect showing the heritable nature of glioma retinae in certain stocks may stimulate more interest in this aspect of the disease, and that observers who meet with multiple cases in the same stock will endeavour to keep such families under observation and report upon their subsequent histories, inquiring always for information concerning collateral branches of the family.

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(γ) INDEX TO CHRONOLOGICAL BIBLIOGRAPHY AND AUTHORS OF PEDIGREES. *GLIOMA RETINAE*

(δ) DESCRIPTIONS OF PEDIGREE PLATES

PLATE XXVI. Fig 333. *Griffith's Case.* (Smith family.) Four cases of hereditary glioma of the retina in a sibship of seven. III. 1, John, aged 5 months, 1903, had both eyes removed for glioma; he died, aged 5, after operation for removal of a tumour in R. upper jaw and palate; secondary growths were found in the kidney. III. 2, Ethel, aged 12, 1917, had both eyes normal. III. 3, Lucy, aged 9 months, 1906, had both eyes removed for glioma; she died, 1907, from measles. III. 4, William, aged 9 months, 1908, had both eyes removed for glioma; he died of this disease two years later. III. 5, stillborn. III. 6, Mary Elizabeth, seen 1913, aged 1 week, no glioma was then seen but it had developed 5 months later, left eye first affected and removed, right eye not removed; child died of broncho-pneumonia 8 months later. III. 7, aged 10 weeks, shows no sign of disease yet. III. 2 and III. 7 were bottle fed and the mother ascribes their immunity to this. II. 2, aged 22, had her right eye removed for a "growth" at the age of 9 months. No consanguinity recorded. Bibl. No. 54.

Fig. 334. *Steinhaus' Case.* Glioma retinae in two generations, five individuals being affected. Thus, in generation II, the third, fifth and sixth born members of a sibship of ten were affected. II. 4, a boy, was operated on in 1875, when he was aged 2 years, for glioma of one retina, this was followed a few months later by recurrence and death. II. 6, a girl, was also operated on in 1877 at the age of 2 years for unilateral glioma retinae; there was no recurrence and the other eye remained healthy; the patient was alive and well in 1900. II. 7, a girl, was operated on for unilateral glioma retinae at the age of 7 years; the tumour was in a late stage of development and she died a few weeks after the operation. Nineteen years after the first case occurred, the eldest brother, II. 2, brought up his daughter, aged 4 years, who was found to have a retinal glioma on the left side; the eye was enucleated (1894) and there had been no recurrence or affection of the right eye. Four years later, 1898, II. 2 brought up his 8 months old son having noticed something wrong with the left eye for a week; a small retinal glioma was found and the eye was enucleated; so far there has been no recurrence or affection of the other eye. No consanguinity recorded. Bibl. No. 33.

Fig. 335. *Thomson and Knapp's Case.* This case was first published in 1874 when the parents, II. 1 and 2, had only two children both of whom had glioma retinae. III. 2, aged 1 year, was seen to have glioma retinae in the R. eye; her parents had noticed a metallic shimmer in the pupil of this eye three months previously; they reported that a brother of the patient, III. 1, had had the same disease; thus a reflex was noticed in the pupil of one eye when he was aged 2 years, six months later the globe ruptured and after another five months the child died; his tumour had been very haemorrhagic and bled at the slightest touch.

At this date (1874), a male cousin on the father's side, III. 8, had died of the same disease in the L. eye when he was aged 2 years; and further an aunt of the father had had two children who died of the same disease between the ages of 2 and 4 years. Macroscopic and microscopic descriptions of the tumour in the case of III. 2 are given.

In 1898 further information of this family is published; the parents II. 1 and 2 had then had fourteen children, five of whom had died of glioma retinae; the aunt, I. 3, had had a third child who had died of the disease, and she herself had died of cancer of the breast. A letter from the mother, II. 1, is quoted as follows—"First child affected with cancer of the eye was a boy born in September, 1869, no medical attendant, he died in August, 1871. The second child was a girl born in August, 1872, disease was noticed in the R. eye in 1873, the eye was removed; seven months later cancer appeared in the other eye and she died in August, 1875. The third child, a boy, was born in 1880; he had cancer in one eye at the age of 3 months and died in 1882. The fourth child, a girl, was born in September, 1883; the disease appeared in her R. eye in 1885 and she died in 1887. The fifth child, a girl, was born in 1888; the disease was noticed in her R. eye in 1890; she died in 1891."

The mother also states that she has five normal sons and four normal daughters. No consanguinity recorded. Bibl. Nos. 21, 32.

Fig. 336. *Caspar's Case.* Glioma retinae in mother and daughter. In 1892, II. 2, aged 2 years, had her L. eye enucleated for glioma retinae; she lived to marry and in 1911 her $1\frac{1}{4}$ years old daughter was noticed to have a similar-looking yellow tumour in her right eye. The eye was enucleated and found to be filled with glioma. I. 1, the mother of II. 2, had a large congenital angioma of the L. upper lid and forehead. No consanguinity recorded. Bibl. No. 45.

Fig. 337. *Pockley's Case.* Glioma retinae in an infant of 18 months. The father, II. 4, had both eyes removed for glioma in infancy and two of his sisters had had both eyes removed "for growths" in infancy. The mother, II. 5, was blind in one eye, there was cataract and no projection, she had also a "partial" cataract in her other eye. Her mother, I. 1, was also blind in one eye from an unknown cause. No consanguinity recorded. Bibl. No. 57.

Fig. 338. *De Gouvea's Case.* Glioma retinae in a father and two daughters. I. 1 had enucleation of his R. eye performed for glioma retinae when he was aged 2 years; the result was excellent and he married at the age of 21. He had seven children, of whom the first was normal; the second, a daughter, had

bilateral glioma retinae and died aged 2 years; the third, also a daughter, had bilateral glioma retinae and died aged 5 months, and the remaining four children are alive and healthy. No consanguinity recorded. Bibl. No. 42.

Fig. 339. *Newton's Case.* Glioma retinae in ten members of a sibship of sixteen. II. 1 died at 6 weeks of bronchitis. II. 2, aged 25, alive and healthy. II. 3, aged 23, alive and delicate. II. 4 had glioma of the R. retina with enucleation performed at $2\frac{1}{2}$ years, local recurrence and death occurred a few weeks later. II. 5 had bilateral glioma retinae which caused rupture of the eyeball and death at 3 years. II. 6, aged 19, alive and healthy. II. 7 died, aged 2, of glioma of L. retina with rupture of the globe. II. 8 died, aged 3, of bilateral glioma retinae with ruptured globes. II. 9 had the right eye enucleated for glioma at the age of $3\frac{3}{4}$ years, death occurred at 5 years from a local recurrence. II. 10 died at 9 months of bronchitis. II. 11 died, aged 3 years, of a bilateral ruptured glioma retinae. II. 12 had bilateral glioma retinae and died at $2\frac{1}{2}$ years from cerebral implication. II. 13, aged 8, alive and healthy. II. 14, also II. 15, died, aged 3 years, of bilateral ruptured glioma retinae. II. 16, the patient was brought up by her mother at the age of 2 years with the story that she had appeared to be blind for fully twelve months. Both pupils were occupied by a mass which completely involved the lens and was growing forward into the anterior chamber. The tension was greatly increased, the globes feeling like balls of wood and the pain was intense, there was no evidence of secondary growths; operation was refused on the prognosis being given. One of the father's brothers was said to have died in infancy of some eye complaint the nature of which could not be determined. No consanguinity recorded. Bibl. No. 35.

Fig. 340. *Hoffmann's Case.* Bilateral glioma retinae in a child aged 1 year. The mother, now aged 28 years, had had her right eye enucleated by Hoffmann's father for glioma retinae at the age of 2 years. No consanguinity recorded. Bibl. No. 40.

Fig. 341. *Taylor's Case.* This case was reported by Johnson Taylor during the discussion following a paper by Snell at a meeting of the Ophthalmological Society in 1905. He said that some years ago he had excised a child's eye for glioma retinae, glioma subsequently developed in the other eye and the child died; the mother of this boy had had an eye excised in early life, and he believed that that also had been for glioma. Bibl. No. 39.

Fig. 342. *Owen and Berrisford's Case.* Six cases of glioma retinae in a small pedigree. I. 2, Thomas Grover, had his left eye removed for glioma retinae when 5 months old in 1859; his son, II. 1, Frank Grover, had one eye removed for glioma by Mr Ridley in 1898 at age of 3 years, he remained well till the age of 15 when he died of "paralysis." I. 3, Beatrice Wallbank, sister to I. 2, had eight children of whom II. 2, Nellie, and II. 3, Charlie, had glioma in both eyes and died aged 4; II. 4, Julia, had glioma in one eye and died aged 4 and II. 7, Gordon, had glioma of both eyes and died aged $3\frac{1}{4}$ years. II. 5, were three normal females, II. 6, a normal male. No consanguinity recorded. Bibl. Nos. 38, 50.

Fig. 343. *Griffith's Case.* (Jones family.) Three cases of hereditary glioma of the retina in a sibship of three born alive. II. 1, stillborn. II. 2, Doris, aged 3 (1906), right eye removed for glioma, now aged 13 with left eye normal. II. 3, George, aged 3 years (1907), right eye removed for glioma, now aged 10 with left eye normal. II. 4, Florence, aged 7 (1913), had right eye removed for glioma, her left eye had been previously removed at age of 1 year and 10 months. All children were breast fed. The mother, I. 2, had her right eye removed for glioma in 1879 at age of $2\frac{1}{2}$ years. No consanguinity recorded. Bibl. No. 54.

Fig. 344. *Von Graefe's Case.* Glioma retinae in a child whose parents were apparently healthy, but several siblings of the mother were said to have died of "Augenkrebs" in their first year of life. No further information is given but there can be no doubt that the "Augenkrebs" of the maternal sibship was glioma retinae. No consanguinity recorded. Bibl. No. 16.

Fig. 345. *Traquair's Case.* Glioma retinae in a father and his two children. I. 1 had his left eye removed "for a tumour" at the age of six months; he survived to marry in 1912. Of his children, II. 1, was stillborn in 1913; II. 2 was born 1914, his parents noticed something wrong with his R. eye at the age of six weeks and at eight months the eye was removed. In June, 1916, glioma of the L. retina appeared and the orbit was exenterated in 1917. Metastases occurred all over the body and death supervened in 1918. II. 3 was born 1916, her parents noticed something wrong in her L. eye at the age of six weeks. Operation was refused and death occurred from broncho-pneumonia soon afterwards. No consanguinity recorded. Bibl. No. 58.

Fig. 346. *Von Graefe's Case.* Glioma retinae in two siblings, the other members of the family healthy. No further information is given. No consanguinity recorded. Bibl. No. 16.

Fig. 347. *Brown's Case.* Glioma retinae in three siblings of a sibship of eight. The parents, aged 40 and 42 respectively, are healthy and have good family histories with no record of cancer or tumours in any of their relatives. III. 1 was seen and glioma was presumably diagnosed in the left retina when he was aged 10 months, the eye was not immediately enucleated as had been advised; five months later signs of the same disease appeared in the right eye and shortly after he became totally blind; he died aged 22 months. The next three children were healthy boys. III. 3, another brother, was seen by the author, who diagnosed

glioma retinae of the left eye when aged $3\frac{1}{2}$ years; the eye was enucleated and the child was well and free from any sign of recurrence two years later. III. 4, a boy, was seen aged 29 months to have some trouble with his left eye, he was taken to the doctor two months later and the eye was enucleated, glioma retinae being again diagnosed; ten months later the child was well and showed no signs of recurrence. Since this time a twin boy and girl have been born who remained healthy and showed no sign of eye trouble at the age of five months. No consanguinity recorded. Bibl. No. 28.

Fig. 348. *Snell's Case.* Two cases of glioma retinae in a sibship of three. III. 1 had both eyes affected, the parents refused operation until it was too late and the patient died. III. 3, aged $4\frac{1}{2}$ months, had glioma of right retina. The parents and their siblings were normal. I. 1 alive and healthy, I. 2 died in childbed, I. 3 and 4 cause of death unknown. No consanguinity recorded. Bibl. No. 36.

Fig. 349. *Wilson's Case.* Glioma retinae in eight siblings. Three of the children died from glioma retinae, one died from a tumour at the base of the brain and the remaining four were still alive when the history was reported. No consanguinity recorded. Bibl. No. 20.

Fig. 350. *Lerche's Case.* Glioma retinae in four children of a sibship of seven. The growth occurred in the left eye of three boys and was bilateral in the case of a girl, II. 2. The parents and three daughters were quite healthy. No consanguinity recorded. Bibl. No. 8.

Fig. 351. *Adam's Case.* II. 1 was seen, aged 2 years, with bilateral glioma retinae; a reflex had been noticed in the left eye since birth; the preauricular and submaxillary glands were enlarged; enucleation was performed but the child died three weeks after operation. Two years later a brother, II. 2, aged 2 years, was seen; he also had bilateral glioma retinae which was more advanced in the right eye than in the left; enucleation was followed by recurrence and death. No information of other siblings is given. No consanguinity recorded. Bibl. No. 44.

Fig 352. *Adam's Case.* Glioma retinae in two brothers. II. 1, seen, aged 2 years, had glioma of the right retina; enucleation was performed and later exenteration of orbit but recurrence and death occurred two years later. II. 2, seen, aged 2 years, had glioma of the right retina, symptoms of which had been present for six months; the orbit was exenterated but recurrence occurred. No information of other siblings. No consanguinity recorded. Bibl. No. 44.

Fig. 353. *Adam's Case.* Glioma retinae in two brothers. II. 1, seen, aged 3 years, had glioma of the right retina with phthisis bulbi of the left eye as a result of septic irido-choroiditis in the first year of life; the R. orbit was exenterated but recurrence occurred and the child died. II. 2, seen, aged 11 months, had glioma of the left retina, a reflex had been noticed in the pupil for several weeks. Enucleation was performed and no recurrence had occurred at the time of the child's death a year later from scarlet fever. No consanguinity recorded. Bibl. No. 44.

Fig. 354. *Snell's Case.* II. 2, aged $2\frac{1}{4}$ years (1905), was brought up by his mother who had noticed a yellow cast in his L. eye since he was aged 3 months and there had been a similar appearance in his R. eye for the last 3 months; the sight was very imperfect in each eye; glioma was diagnosed and both eyes were removed; there had been no recurrence up to date. The mother had had one other child, II. 1, who had had bilateral glioma and had had one eye removed; she died aged $2\frac{3}{4}$ years. The diagnosis was confirmed by microscopic examination. No consanguinity recorded. Bibl. No. 39.

Fig. 355. *Schoenemann's Case.* Glioma retinae in two brothers with four normal siblings and healthy unrelated parents. II. 2 was seen, aged 3 years, with glio-sarcoma of the right eye in an advanced condition, the parents had noticed it two years previously; the tumour was extirpated, but metastases were present and death occurred. II. 3 was seen, aged 10 months, when glioma retinae at an early stage was diagnosed in the left eye; the eye was enucleated and no recurrence had occurred when the child died of diphtheria six months later. No consanguinity. Bibl. No. 23.

Fig. 356. *Calderini's Case.* Glioma retinae in three siblings. II. 3, aged 6, was seen with glioma of the L. retina which had been first noticed eleven months previously; the eye was excised, but the child died four days after the operation of suppurative meningitis. Her two sisters had already died from glioma retinae, one of them after a long illness and the other from a recurrence after operation. Eight siblings remained free from eye disease but died of phthisis. No consanguinity recorded. Bibl. No. 15.

Fig. 357. *Wintersteiner's Case.* Glioma retinae in two siblings. II. 2, seen, aged 2 years, had been blind in his R. eye since birth, the other eye being normal; glioma retinae was diagnosed and the eye enucleated; the boy died a month later of meningitis. A brother was reported to have died of the same disease. The author gives a very full account of the macroscopic and microscopic appearances of the excised eye. No consanguinity recorded. Bibl. No. 31.

Fig. 358. *Macgregor's Case.* Glioma retinae in three members of a sibship of five; the father was living and in good health, the mother died, aged 34, of "disease of the liver and heart." II. 1 had the L. eye removed at the age of 2 years, the tumour recurred in the stump, the R. eye became affected and the child died. II. 2 had the L. eye removed at the age of 3 months, nine months later the R. eye became affected and the child died after a few months. II. 3, aged 6 years, was healthy. II. 4, a boy, aged 4 years, was

seen with a large tumour of the R. eye, the L. eye had been removed at the age of 17 months and it was nearly 2 years later before the R. eye became affected; he died a few days after admission to hospital. II. 5, aged 15 months, had no symptoms of glioma retinae. No consanguinity recorded. Bibl. No. 25.

Fig. 359. *Sichel's Case.* Glioma retinae in four children of a sibship of five. The parents were well and had excellent health and there was no cancer known in the family of either of them. They had already lost two children from "cancer of the eye" when the mother brought up Pierre C., II. 4, aged $3\frac{1}{2}$ years, in 1835 for an affection of his R. eye. The pupil was dilated and immobile, the iris greyish and slightly discoloured, the reflex known as "amaurotic cat's eye" was present and vision was completely abolished. Operation was urged and refused by the parents who had seen recurrence after operation in a former child. When it was too late the parents asked for operation, which was performed and followed by recurrence and death. A detailed account of the autopsy and microscopical appearance of the growth is given. After the death of II. 4 another male child was born. His mother brought him up when he was several months old and his eyes were perfectly healthy. In 1839, when he was aged about 14 months, glioma was noticed in his L. eye. Operation was refused and the condition progressed until the child died. No consanguinity recorded. Bibl. No. 12.

Fig. 360. *Comas' Case.* Five cases of glioma retinae in a sibship of eleven. The affected members were three females and two males of whom only one, a male, was still alive; he, now aged 12, was enjoying good health, though blind, both eyes were enucleated, one at the age of 2 years, and the right eye 6 months later, the resection of the palpebral conjunctiva and suture of eyelids had also been performed. There had been eight enucleations and five operations for recurrence in members of this family. The father died of gastric cancer; the mother and six living children were in good health. No consanguinity recorded. Bibl. No. 59.

Fig. 361. *De Haas' Case.* Glioma retinae in the left eye of a child who had had its right eye enucleated for the same disease three years previously. The author's father had removed the right eye of the child's father for glioma retinae in 1882. No further information concerning the family history is given. No consanguinity recorded. Bibl. No. 51.

Fig. 362. *Maher's Case.* In 1896 the author was consulted about the eyes of II. 2, James H., aged 18 months; he had glioma of the R. retina and the eye was enucleated; a few weeks later the L. eye was enucleated for the same condition. II. 3, Marion H., had both eyes removed for glioma retinae at the age of 2 years. II. 4, Isabella H., had her L. eye removed for glioma retinae at the age of 1 year. All the four children of this sibship were seen by the author at the ages of 8, 7, 5 and $3\frac{1}{2}$ years respectively when they were in excellent health. It is possible that this is the same family as the one described by Pockley in 1919 (see Fig. 337). No consanguinity recorded. Bibl. No. 34.

Fig. 363. *Fuchs' Case.* Glioma retinae in two children of a sibship of three, the third child, II. 3, when seen aged a few months, having a congenital coloboma of the iris downward as well as a coloboma of the choroid. II. 1 was seen when aged 4, and operated on; he died of a recurrence about 6 months later. II. 2 was operated on when aged 2; he died of a recurrence about a year later. No consanguinity recorded. Bibl. No. 37.

Fig. 364. *Boyd's Case.* In a discussion on the family history of glioma retinae presented by Thomson (see Fig. 335), Boyd reports that he had a case, II. 3, whose brother and sister had died of the same disease; his case also died and thus three out of five children in this family had died of glioma retinae. The parents were both healthy. No consanguinity. Bibl. No. 32.

Fig. 365. *Zinke's Case.* Glioma retinae in two brothers. II. 1 was reported to have commenced to squint with the left eye at the age of six months, subsequently loss of vision, protrusion of the eye and sudden death occurred. II. 2 represents three healthy siblings. II. 3 began to squint with the left eye at the age of six months, the condition remained stationary for a year during which time the child appeared to be otherwise in perfect health; an attack of diphtheria was associated with an acute inflammatory condition which developed in the left eye and which did not subside, vision was lost but the child was not taken to a surgeon until he was aged 4 years when there was a large tumour projecting from the orbit and he was suffering severe pain; gradual loss of sight had also been noticed in the right eye and on examination an intra-ocular tumour was found on this side also. The left eye was enucleated but a rapid recurrence and metastases occurred and the child died six months after the operation. The father was dead, cause not stated, the mother was insane. No consanguinity recorded. Bibl. No. 22.

Fig. 366. *Purtscher's Case.* Five cases of glioma retinae in two generations. The father, I. 1, died of sarcoma of the thorax, the mother, I. 2, was healthy. Of their eleven children, II. 1, Karl, aged 32, was normal; II. 2, Ludmilla, was normal, and had three normal children, two boys and one girl; II. 4, Josefa, aged 30, was first examined at the age of 20 (1907), she had seen badly with the left eye in childhood and suffered from severe headaches; her left vision was reduced to finger counting at $\frac{3}{4}$ m. to the temporal side and this was found to be due to a large sharply bounded white area with vandyked edges, in many places pigmented, situated upwards, outwards and below the optic disc; the diagnosis was held to be between

choroiditis and a neoplasm; she was seen again in 1914 and in 1915 was recommended to the Fuchs' clinic in Vienna where a diagnosis of arrested glioma was made; a small atrophic area indicating the same condition was also found in the right eye. II. 5, Josef, aged 29, was normal; II. 6, Thomas, died aged 1 year; II. 7, Johanna, aged 25, was reported to have not very good sight; II. 8, Ella, aged 24, herself normal, had two boys with glioma retinae; II. 10, Hubert and II. 11, Therese, aged 23, were normal; II. 12, Engelbert, died, aged $9\frac{1}{4}$ years, of bilateral glioma retinae and II. 13, Ferdinand, died, aged 2 years and 8 months, of bilateral glioma retinae.

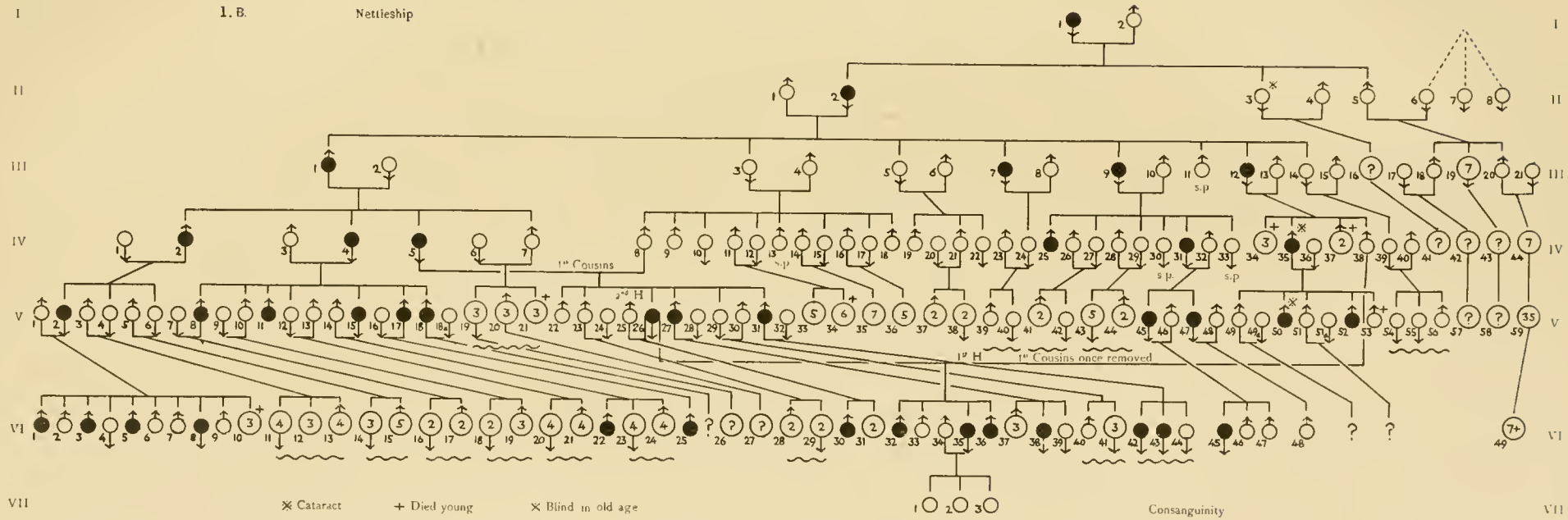
Of the two affected children of Ella, III. 5, Walther, died, aged $3\frac{1}{4}$, of glioma retinae; III. 4, Karl, aged 5, was first seen, aged 4, when his left vision was reduced to finger counting and a yellowish white mass, slightly prominent, occupied the macula region; he was seen at the Fuchs' clinic and an arrested gliomatous process was diagnosed; there was ophthalmoscopic evidence of a similar condition in the right eye. No consanguinity recorded. Bibl. No. 49.

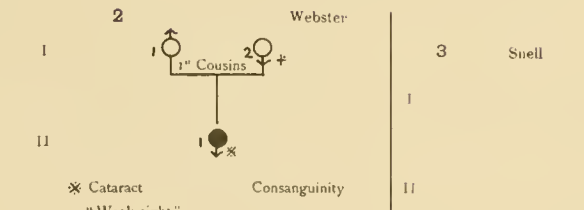
PLATE XXII. Fig. 298. *Flexner's Case.* Glioma retinae in three siblings. II. 1 had an eye enucleated at the age of 6 months for this disease; this was followed by a recurrence and death. II. 2, aged 4 months, had an eye enucleated for glioma retinae which was first noticed by the parents five weeks previously; two weeks after operation the disease appeared in the other eye, the parents refused operation and the child was not seen again. Two years later, II. 3, aged 4 months, was seen with glioma retinae; the parents refused operation and the child died. The author does not refer to any normal siblings. There was no history of malignant disease in the ancestry of the children; the father was alcoholic at one time and had a consequent amblyopia which is the only record of eye disease in the family. The author gives a detailed account of the pathology of the growth in the case of II. 2. No consanguinity recorded. Bibl. No. 29.

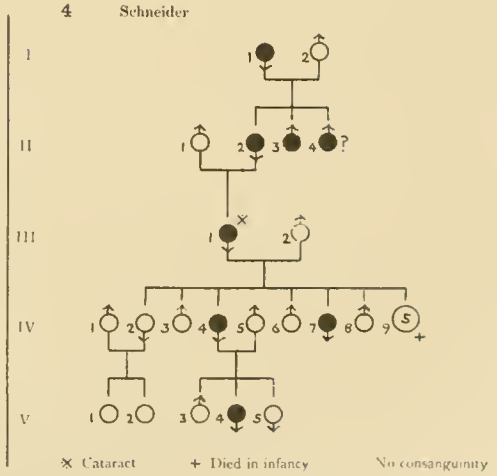
Fig. 299. *Marshall's Case.* Three cases of glioma retinae in a sibship of six. II. 6, Ada Lydia W., aged 2 years, was brought up with a history that for about 2 months a whitish appearance had been seen in the right eye; glioma was diagnosed and the eye excised. On examination under chloroform a glioma was seen in the left eye; further operation was refused by the parents and the child died suddenly in convulsions after about 7 months. A white mass was seen inside the eye of II. 1, at about 2 years of age; no operation was performed and she became worse until the eye ruptured and she died in convulsions, aged $3\frac{1}{2}$ years. II. 2 died in convulsions, aged 3 months; eyes not examined. II. 3 had his right eye removed for glioma when aged about 9 months; at the age of 15 years, he had good sight in the left eye and excellent health. II. 4 and 5, aged 9 and 7 years respectively, are normal. No consanguinity. Bibl. No. 30.

PEDIGREE PLATES

NOS. I–XXVI







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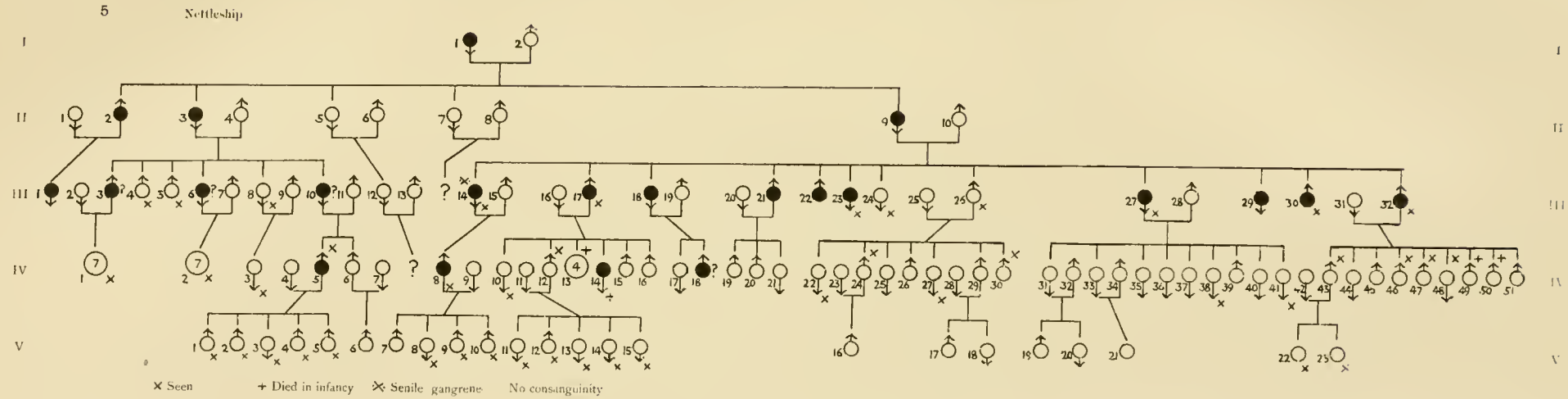

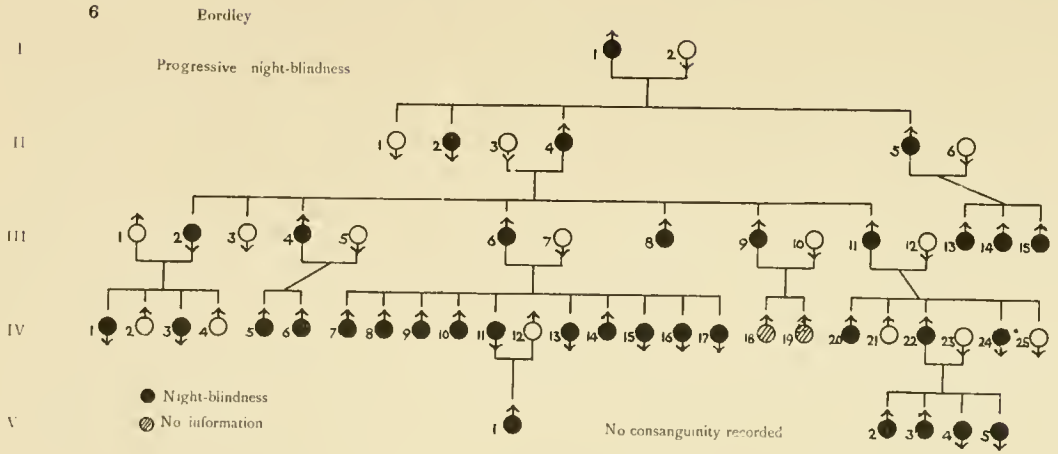

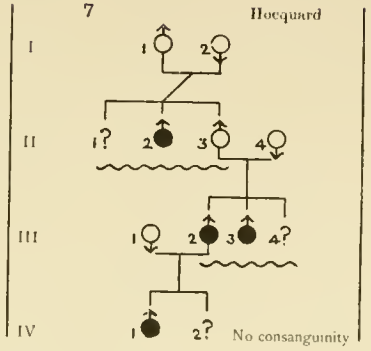

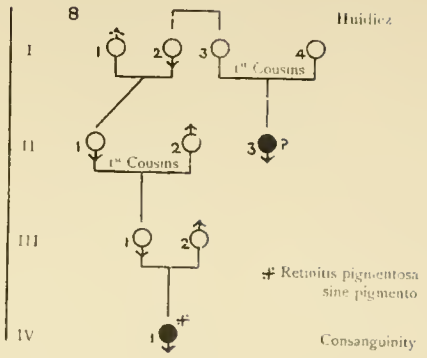

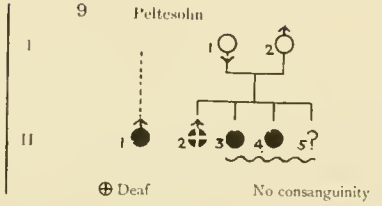

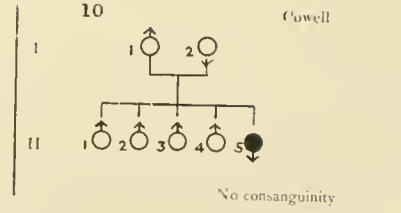

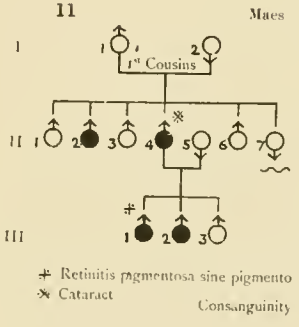

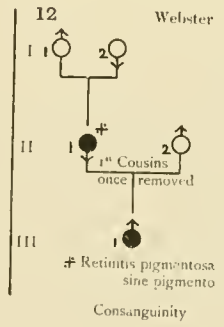

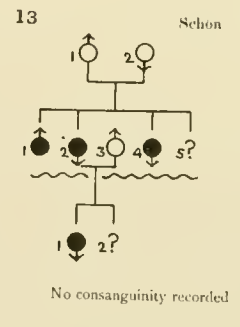

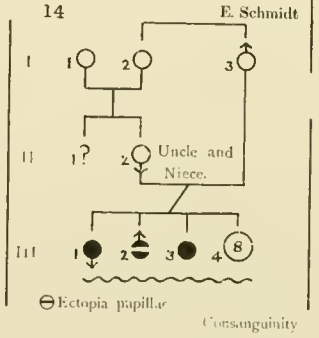

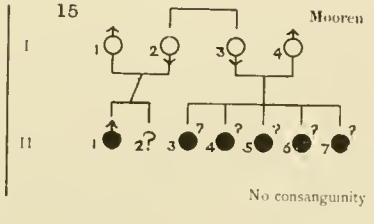

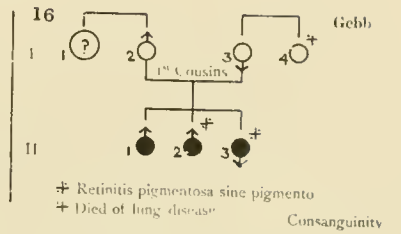

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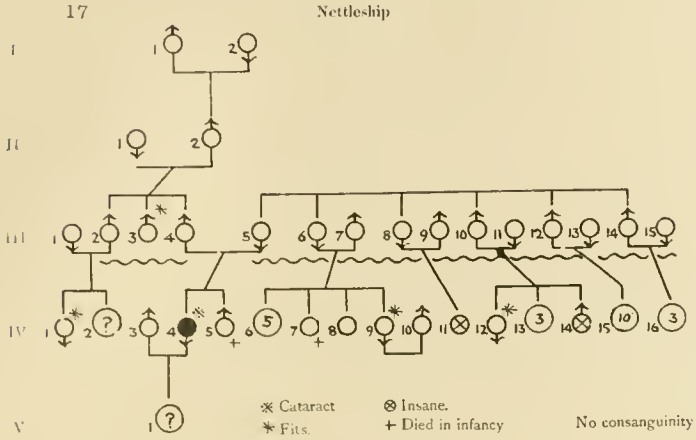
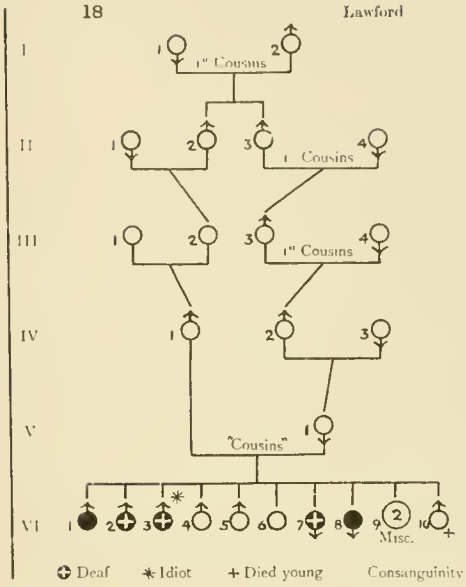
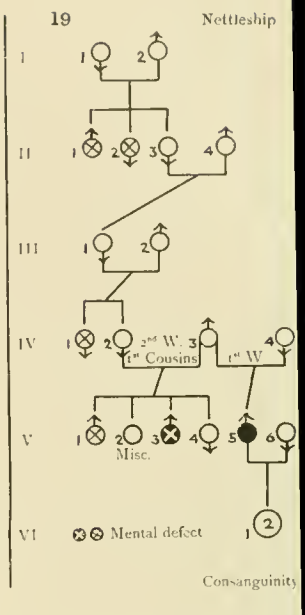
17 Nettleship



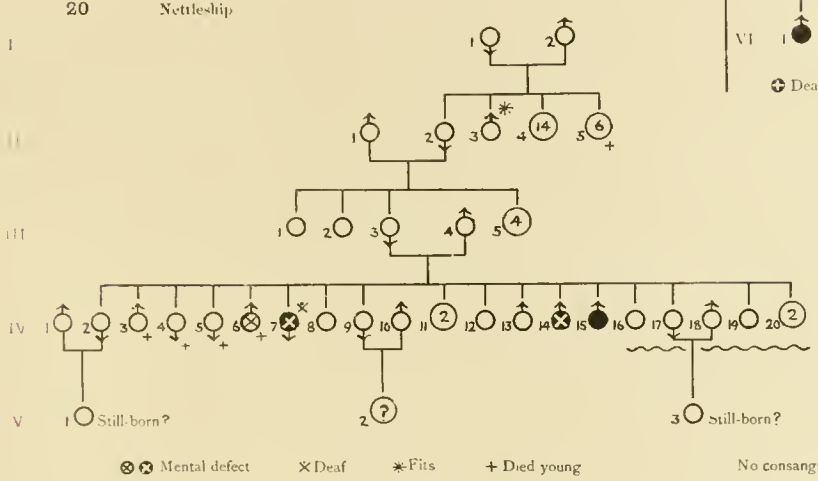
18 Lawford



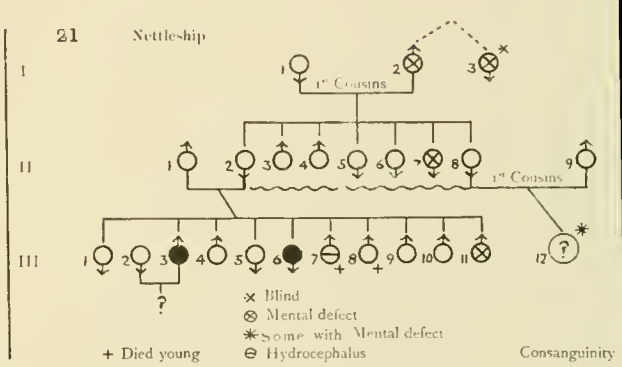
19 Nettleship



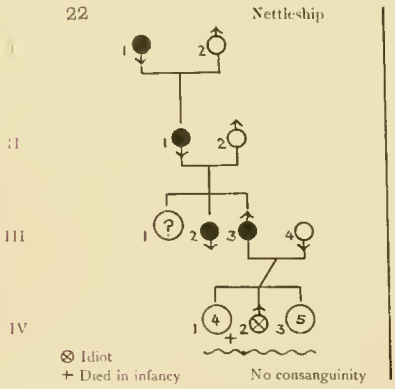
20 Nettleship



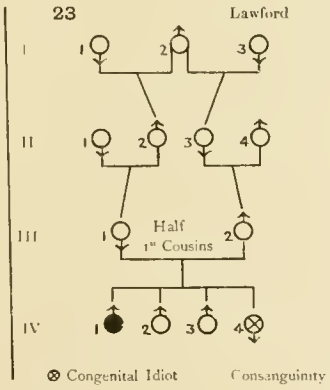
21 Nettleship



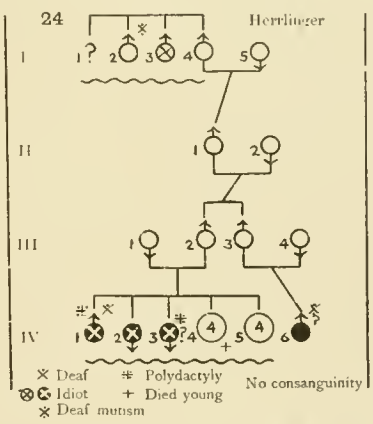
22 Nettleship



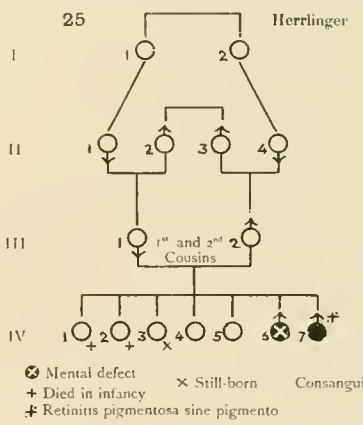
23 Lawford



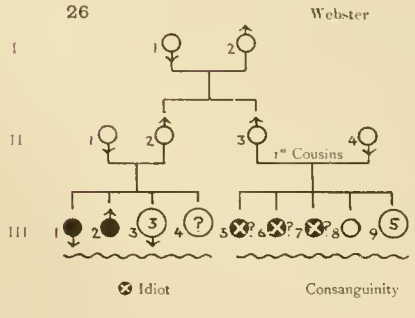
24 Herrlinger



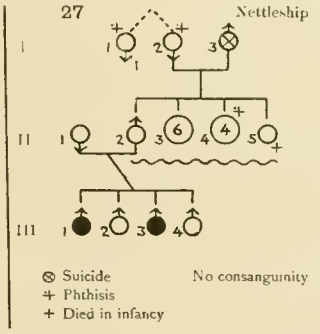
25 Herrlinger



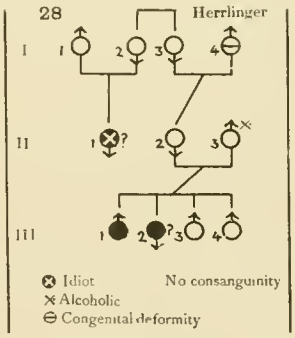
26 Webster



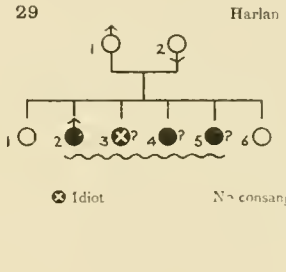
27 Nettleship

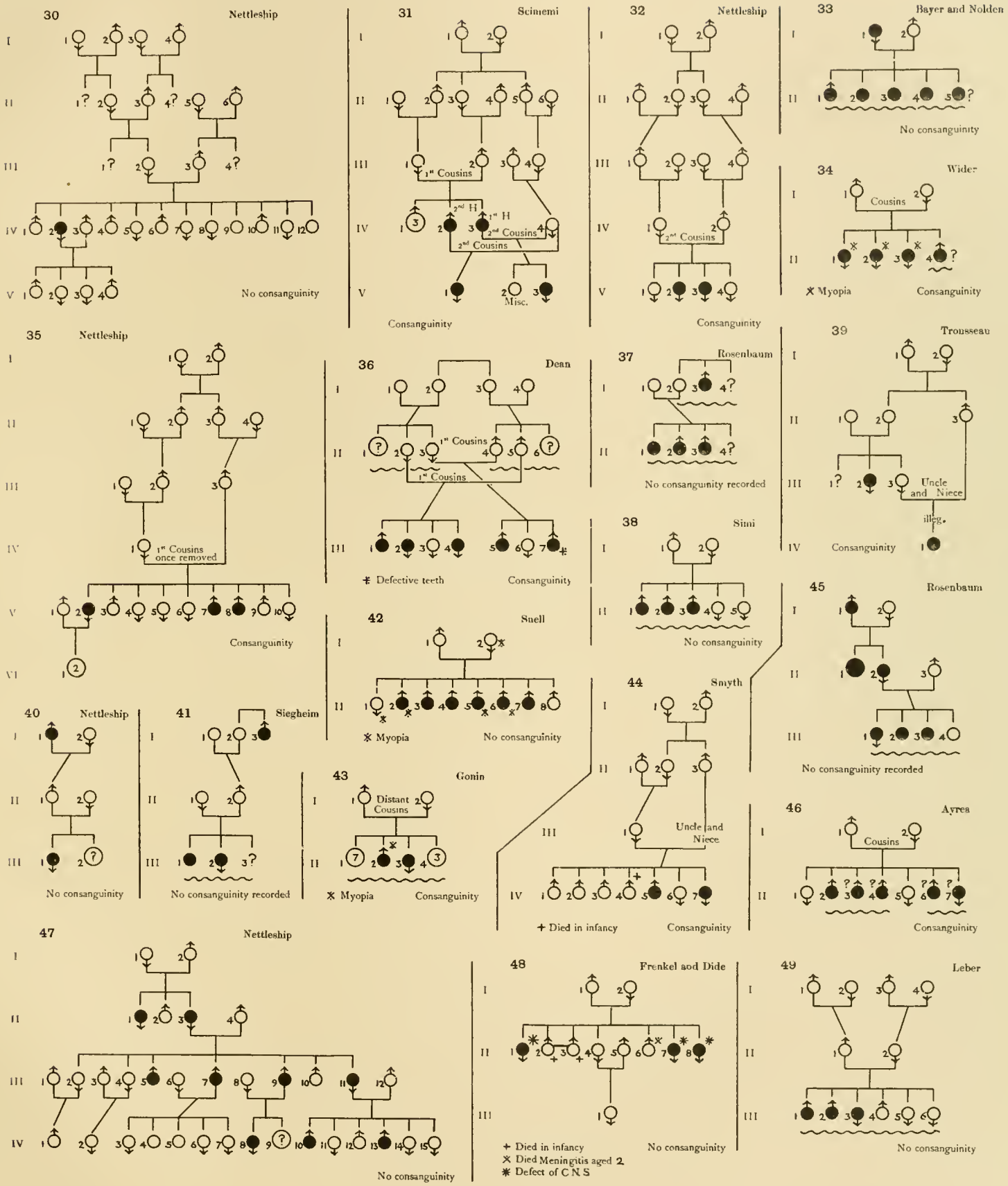


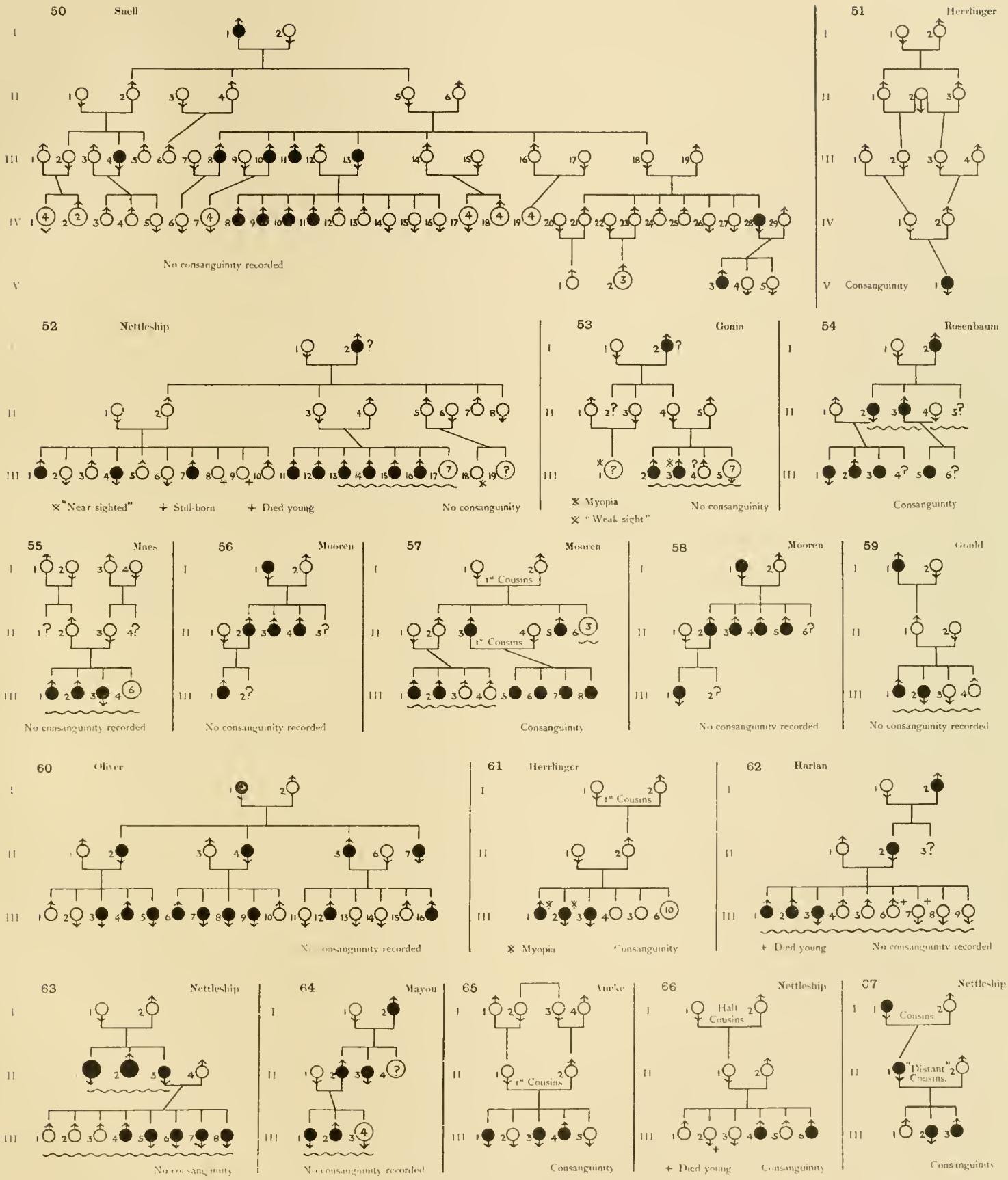
28 Herrlinger

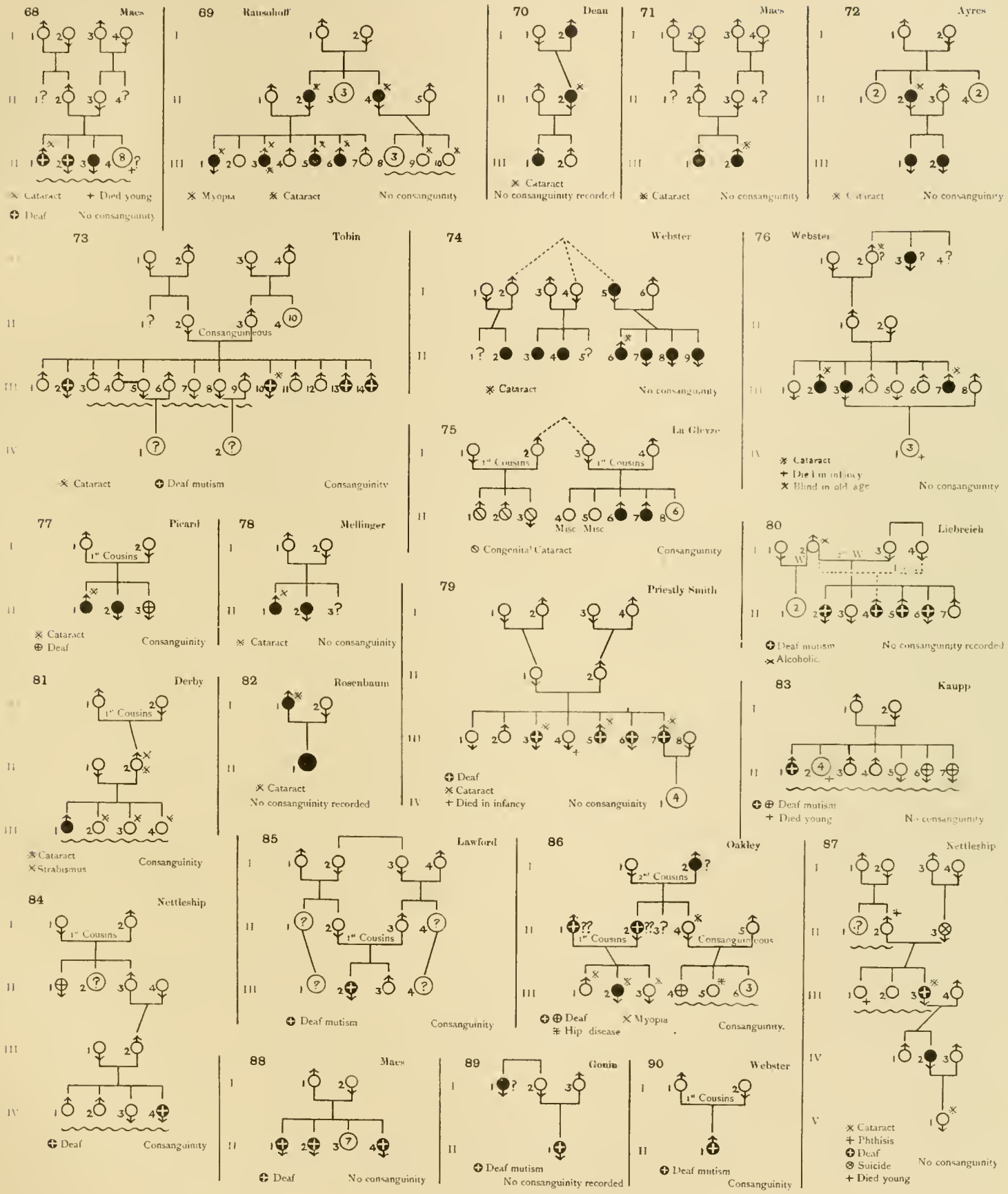


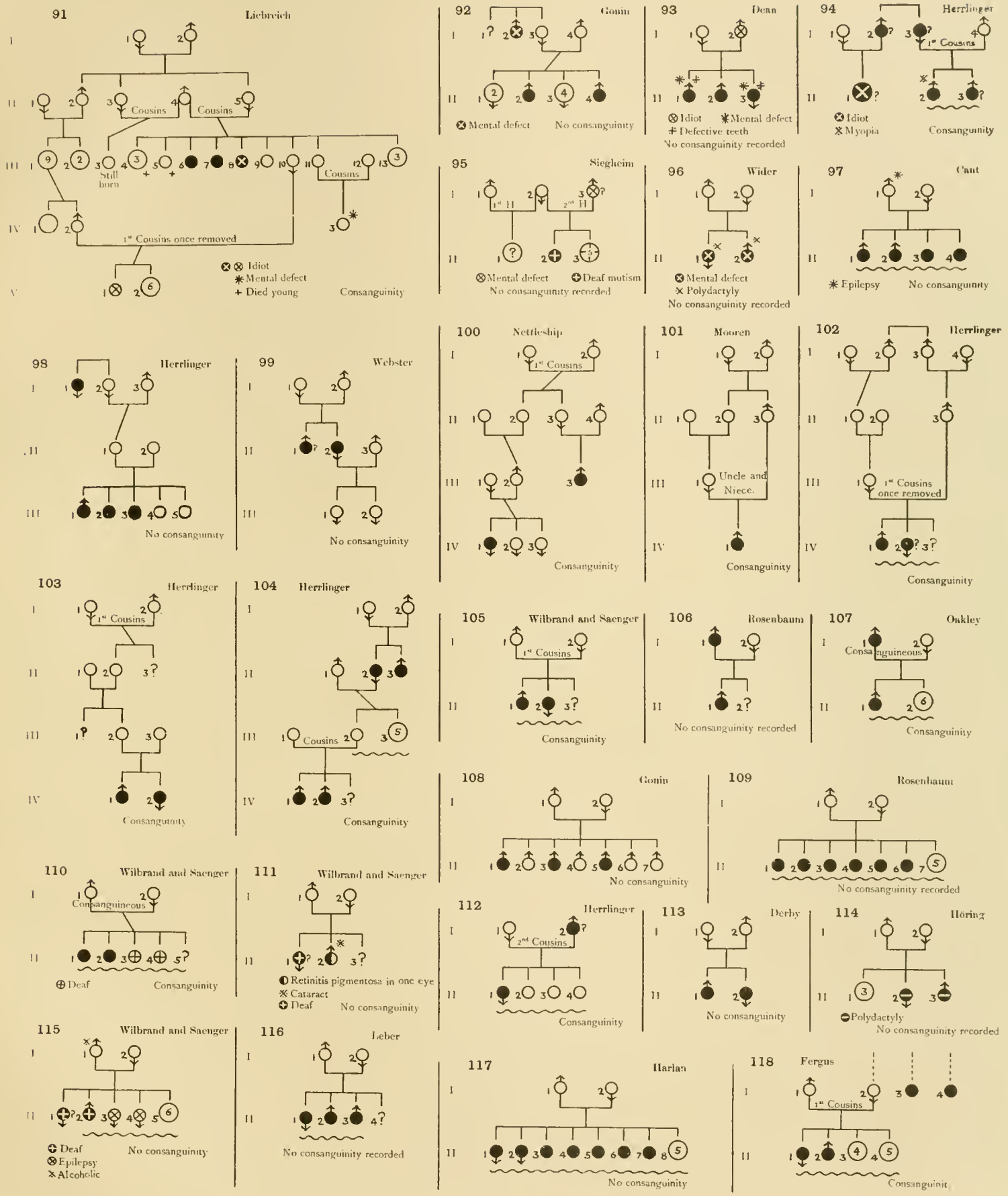
29 Harlan




30 Nettleship
No consanguinity
31 Scimemi
1st Cousins
2nd H
1st H
2nd Cousins
2nd Cousins
Misc.
Consanguinity
32 Nettleship
2nd Cousins
Consanguinity
33 Bayer and Nolden
No consanguinity
34 Wider
Cousins
Myopia
Consanguinity
35 Nettleship
1st Cousins once removed
Consanguinity
36 Dean
1st Cousins
1st Cousins
Defective teeth
Consanguinity
37 Rosenbaum
No consanguinity recorded
38 Simi
No consanguinity
39 Trousseau
Uncle and Niece illeg.
Consanguinity
40 Nettleship
No consanguinity
41 Siegheim
No consanguinity recorded
42 Snell
Myopia
No consanguinity
43 Gonin
Distant Cousins
Myopia
Consanguinity
44 Smyth
Uncle and Niece
Died in infancy
Consanguinity
45 Rosenbaum
No consanguinity recorded
46 Ayres
Cousins
Consanguinity
47 Nettleship
No consanguinity
48 Frenkel and Dide
Died in infancy
Died Meningitis aged 2
Defect of CNS
No consanguinity
49 Leber
No consanguinity


50 Snell
No consanguinity recorded
51 Herrlinger
Consanguinity
52 Nettleship
"Near sighted" + Still-born + Died young
No consanguinity
53 Gonin
Myopia
"Weak sight"
No consanguinity
54 Rosenbaum
Consanguinity
55 Maes
No consanguinity recorded
56 Mooren
No consanguinity recorded
57 Mooren
1st Cousins
1st Cousins
Consanguinity
58 Mooren
No consanguinity recorded
59 Gould
No consanguinity recorded
60 Oliver
No consanguinity recorded
61 Herrlinger
1st Cousins
Myopia
Consanguinity
62 Harlan
+ Died young
No consanguinity recorded
63 Nettleship
No consanguinity
64 Mayou
No consanguinity recorded
65 Vancke
1st Cousins
Consanguinity
66 Nettleship
Half Cousins
+ Died young
Consanguinity
67 Nettleship
Cousins
"Distant" Cousins.
Consanguinity


68 Maes
Cataract + Died young
Deaf No consanguinity
69 Rausahoff
Myopia Cataract No consanguinity
70 Dean
Cataract
No consanguinity recorded
71 Maes
Cataract No consanguinity
72 Ayres
Cataract No consanguinity
73 Tobin
Consanguineous
Cataract Deaf mutism Consanguinity
74 Webster
Cataract No consanguinity
75 Le Gleyze
1st Cousins 1st Cousins
Misc Misc
Congenital Cataract Consanguinity
76 Webster
Cataract
+ Died in infancy
Blind in old age No consanguinity
77 Picard
1st Cousins
Cataract
Deaf Consanguinity
78 Mellinger
Cataract No consanguinity
79 Priestly Smith
Deaf
Cataract
+ Died in infancy No consanguinity
80 Liebreich
Deaf mutism No consanguinity recorded
Alcoholic
81 Derby
1st Cousins
Cataract
Strabismus Consanguinity
82 Rosenbaum
Cataract
No consanguinity recorded
83 Kaupp
Deaf mutism
+ Died young No consanguinity
84 Nettleship
1st Cousins
Deaf Consanguinity
85 Lawford
1st Cousins
Deaf mutism Consanguinity
86 Oakley
2nd Cousins
1st Cousins Consanguineous
Deaf Myopia
Hip disease Consanguinity
87 Nettleship
Cataract
+ Phthisis
Deaf
Suicide
+ Died young No consanguinity
88 Maes
Deaf No consanguinity
89 Gonin
Deaf mutism
No consanguinity recorded
90 Webster
1st Cousins
Deaf mutism
Consanguinity



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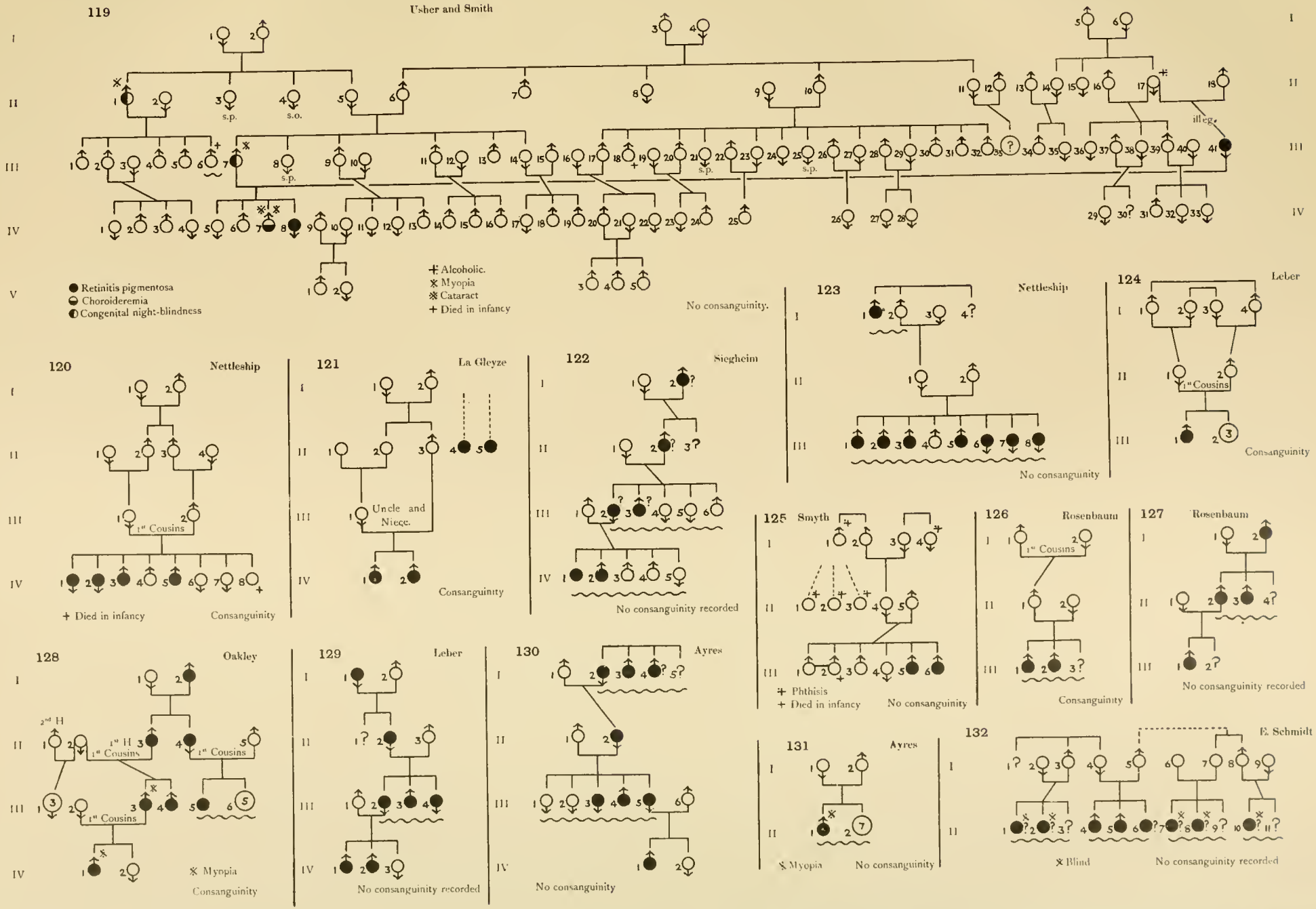

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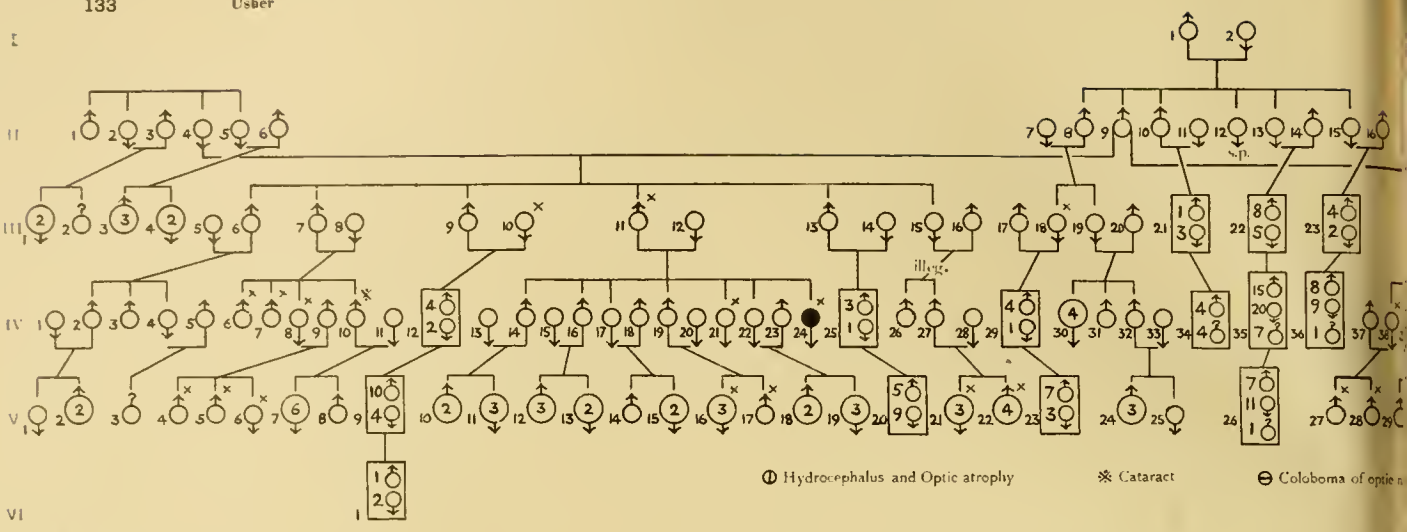
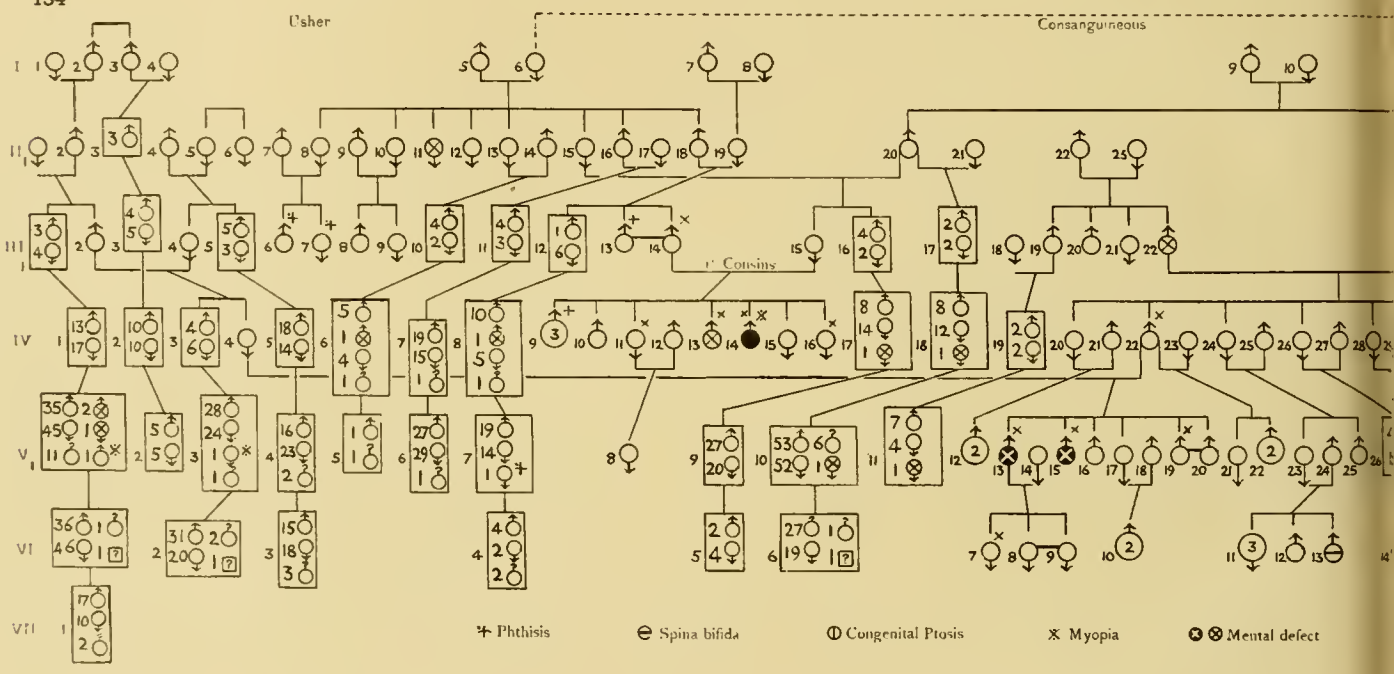
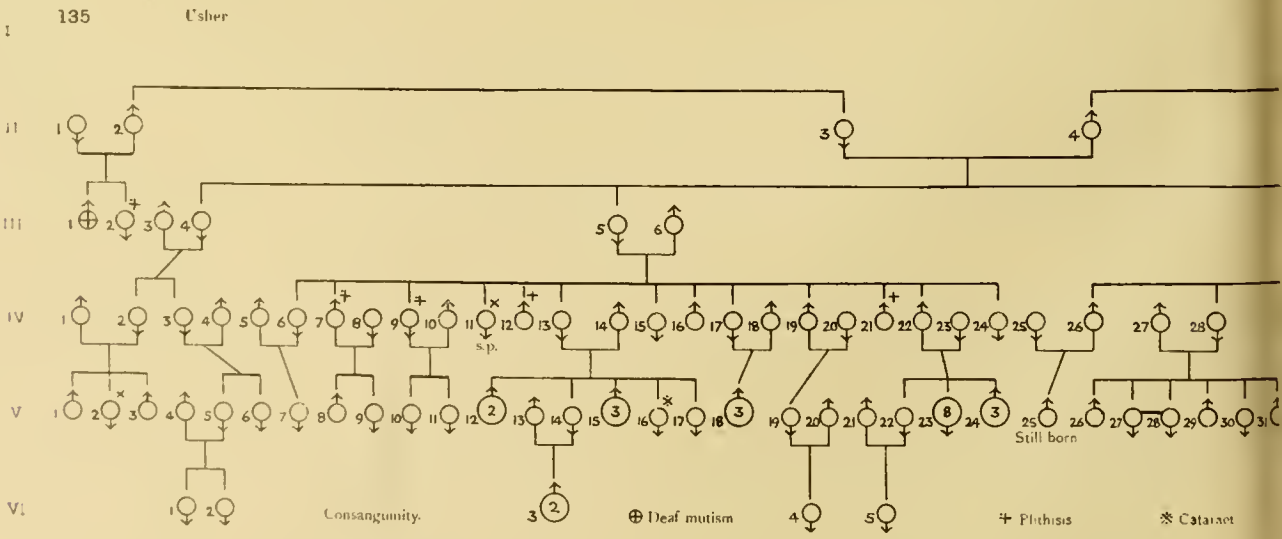
133 Usher

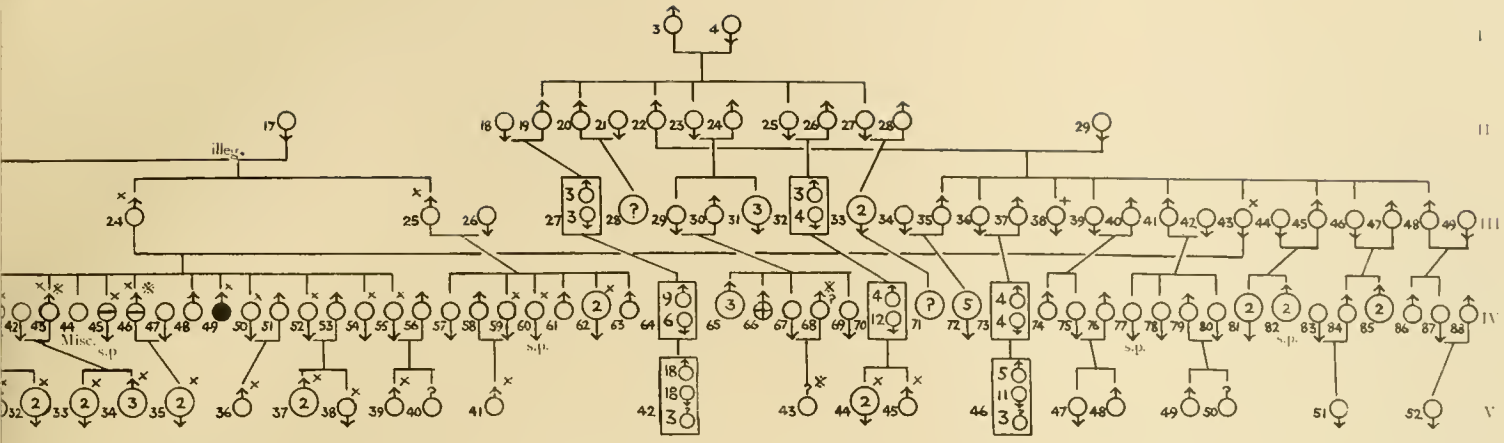


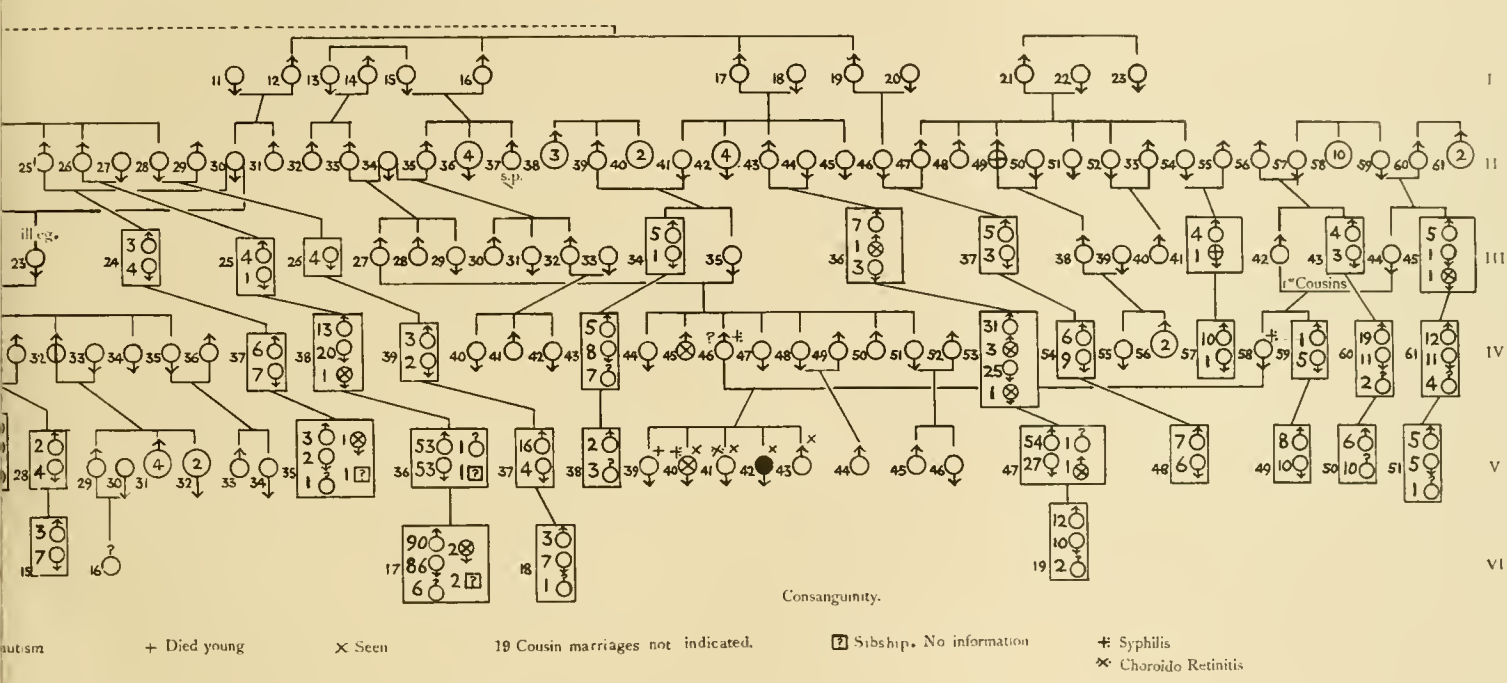
134 Usher

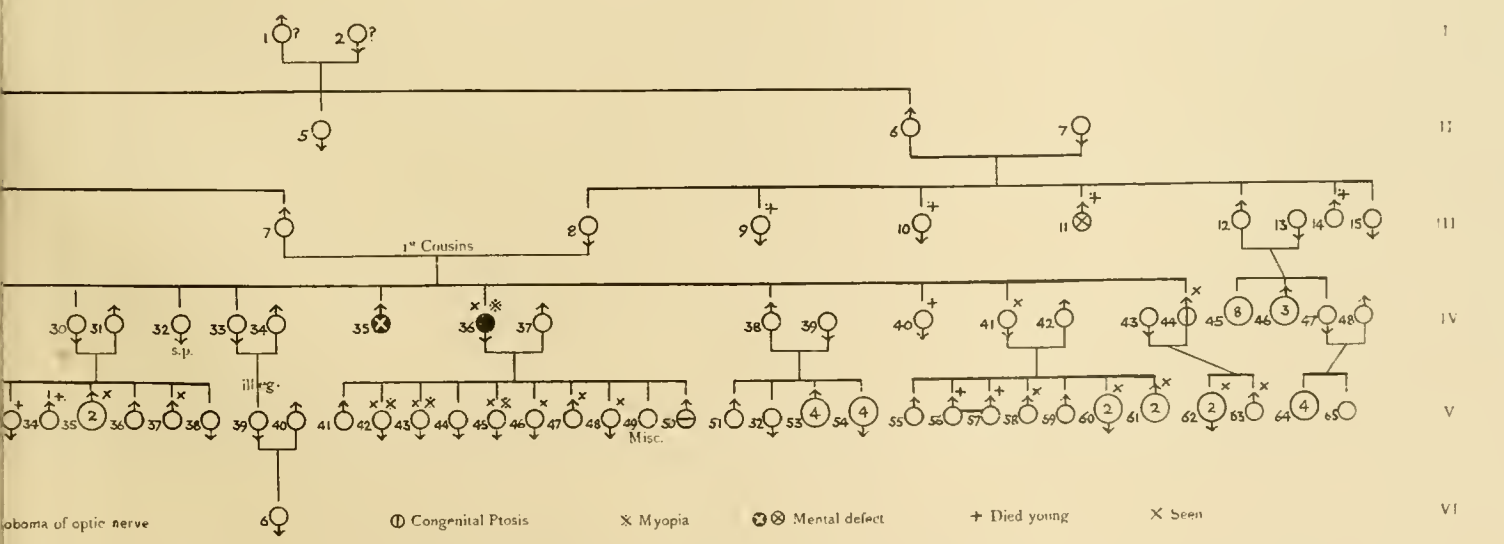


135 Usher



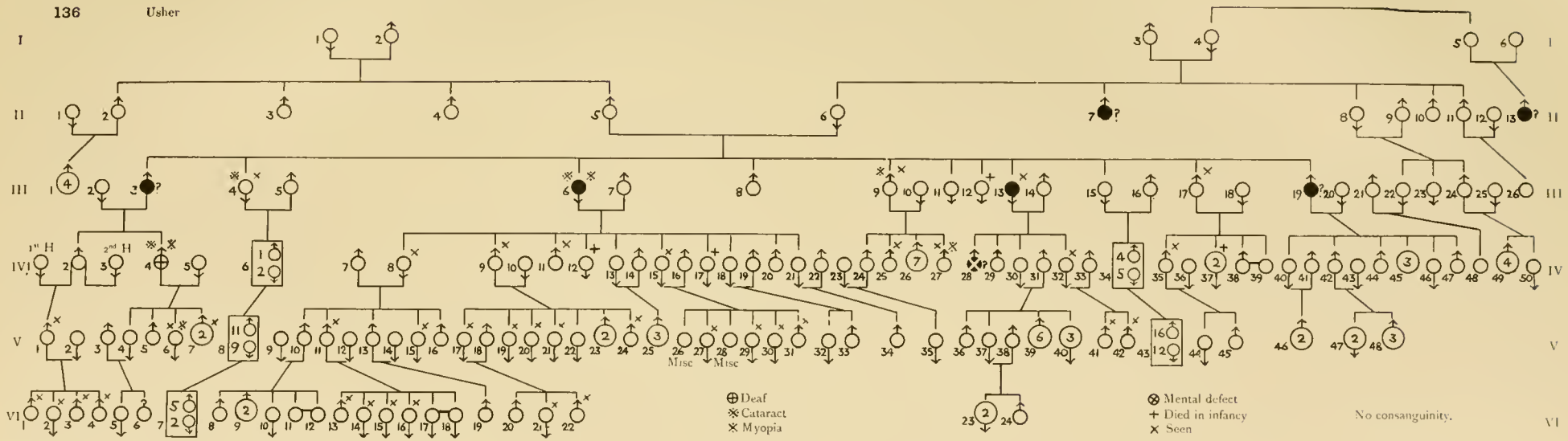




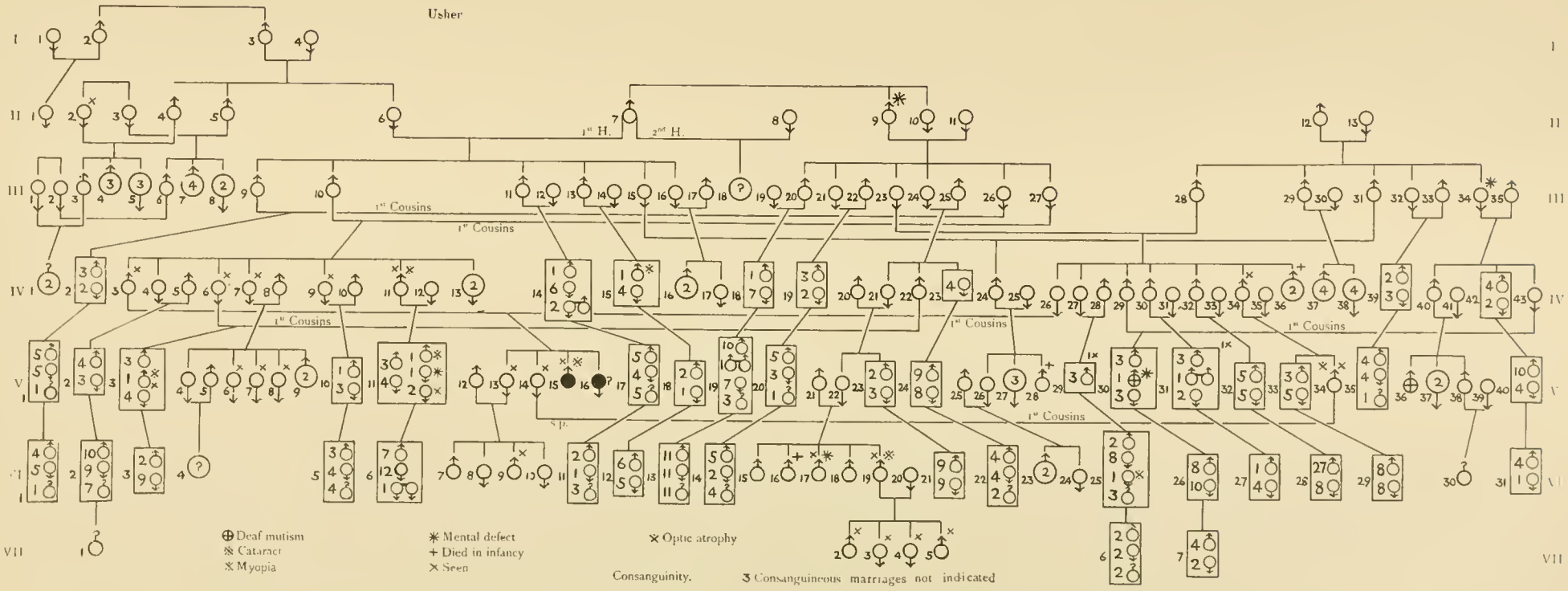


Issued by the Francis Galton Laboratory for National Eugenics.

136 Usher



137 Usher



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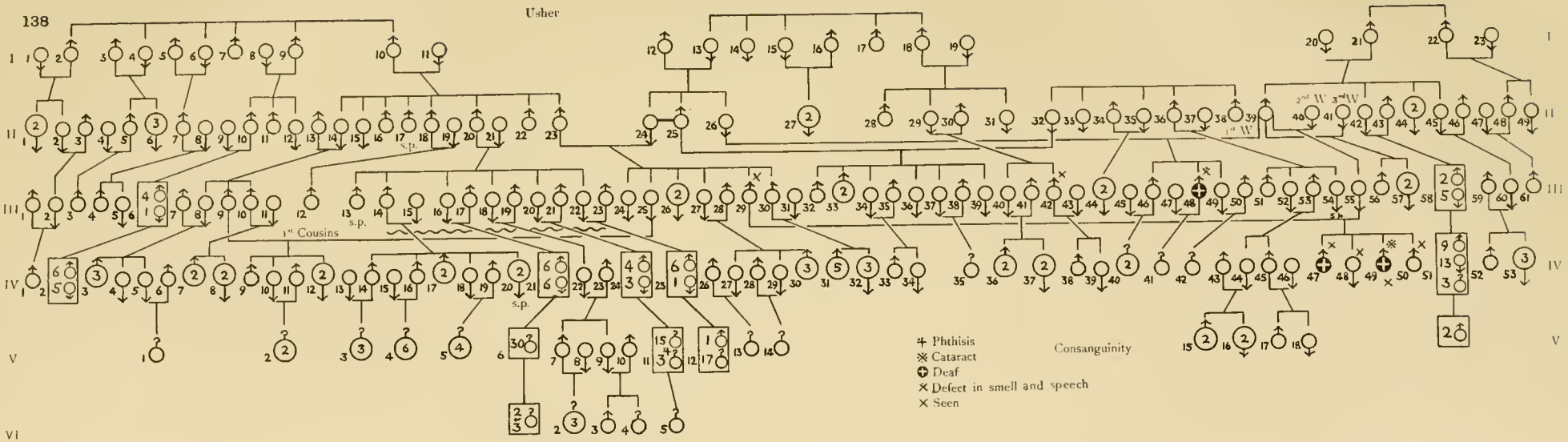
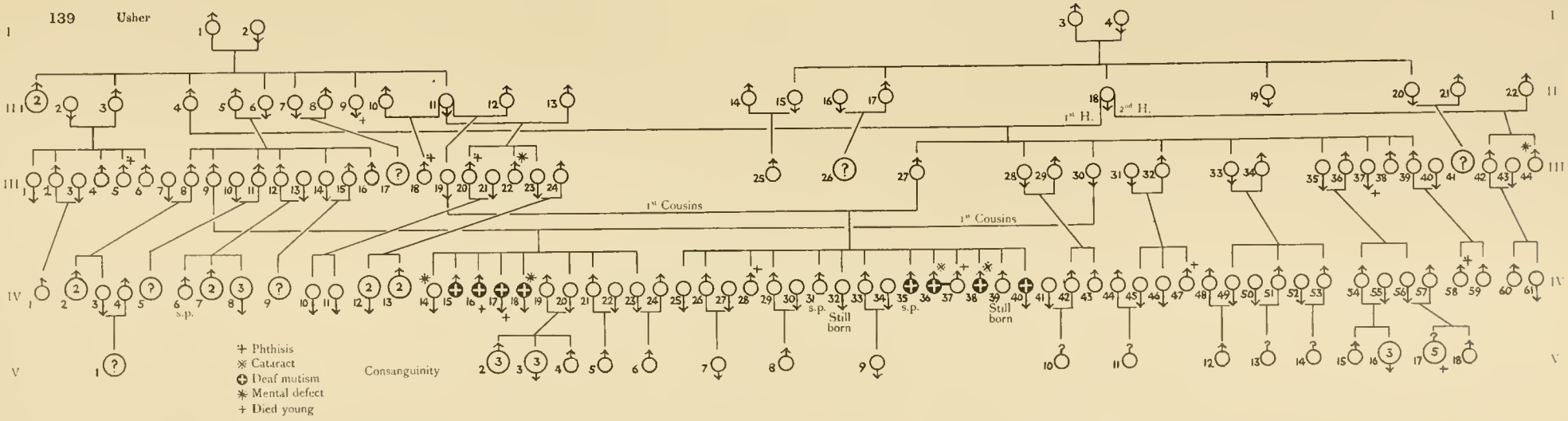
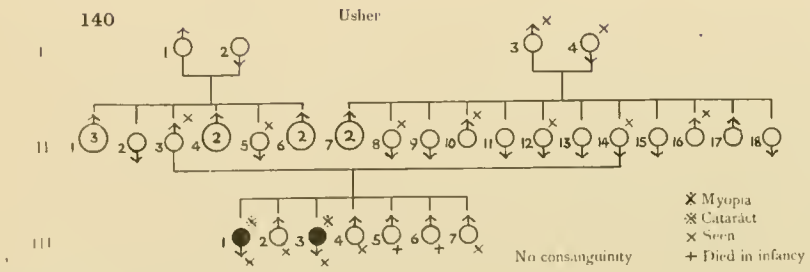
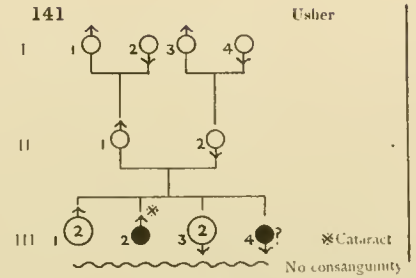
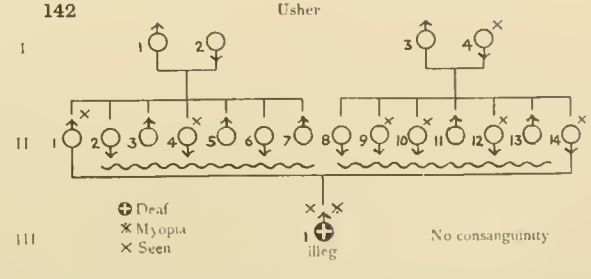

138
Usher
1st Cousins
s.p.
Consanguinity
Phthisis
Cataract
Deaf
Defect in smell and speech
Seen


139
Usher
1st H.
2nd H.
1st Cousins
s.p.
Still born
Consanguinity
Phthisis
Cataract
Deaf mutism
Mental defect
Died young


140
Usher
Myopia
Cataract
Seen
Died in infancy
No consanguinity


141
Usher
Cataract
No consanguinity


142
Usher
Deaf
Myopia
Seen
illeg
No consanguinity

143 Usher

※ Cataract
※ Epilepsy
⊖ Goitre

⊗ Mental defect
+ Died young
× Seen

No consanguinity.

144 Usher

illeg.

Still-born

illeg.

Misc.

Misc.

Misc.

illeg.

⊖ Hare lip
※ Cataract
※ Myopia

⊗ Mental defect
+ Died young
× Seen

⊕ Deaf mutism
ǂ Had 4 Deaf mute cousins.

No consanguinity

145 Usher

illeg.

illeg. illeg

+ Phthisis
※ Myopia
⊗ Mental defect

ǂ Tubercular.

ǂ Syphilis
+ Died young
× Seen

No consanguinity.

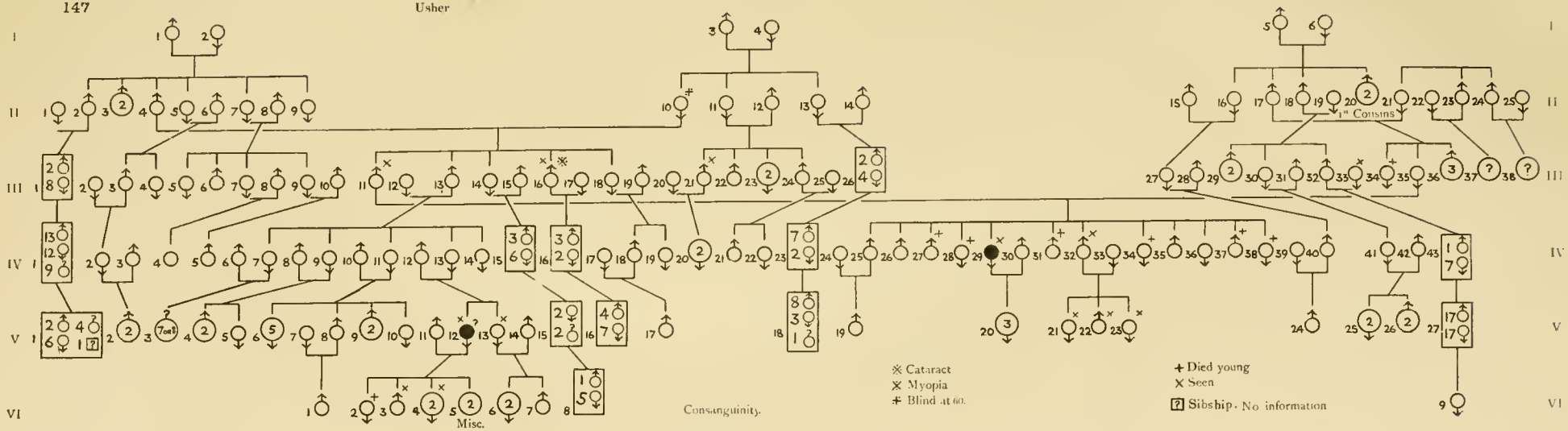
146 Usher

Still born

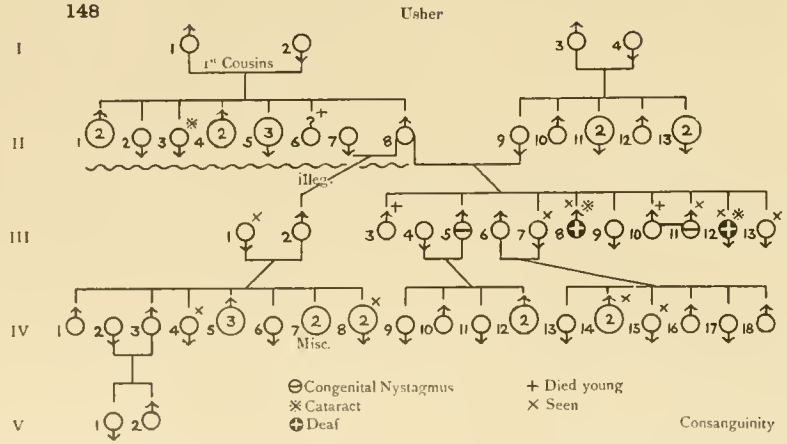
※ Cataract
※ Myopia
+ Died in infancy
× Seen

No consanguinity.

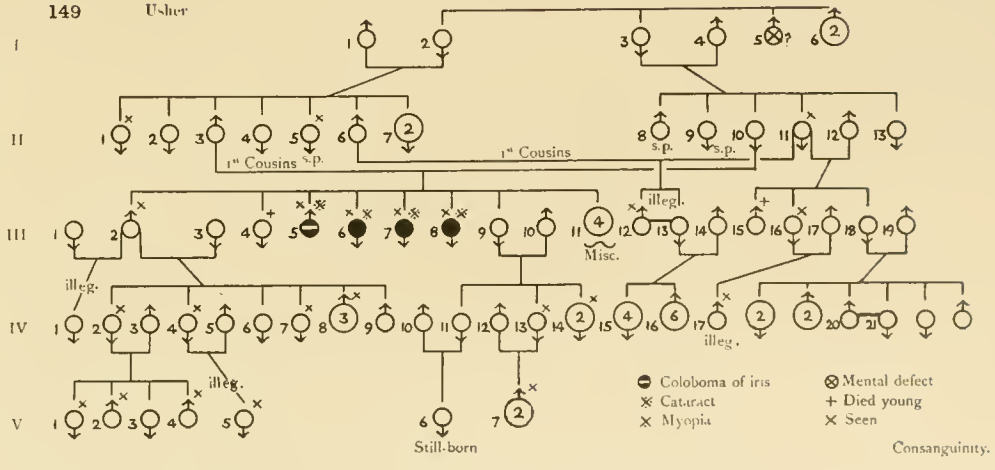
147 Usher



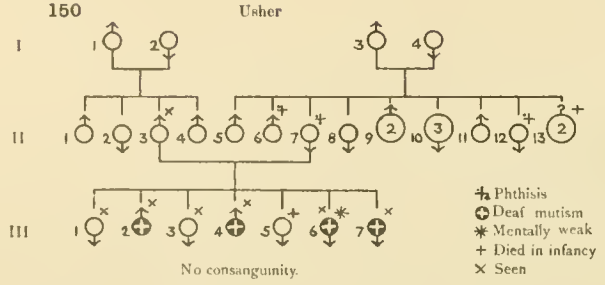
148 Usher



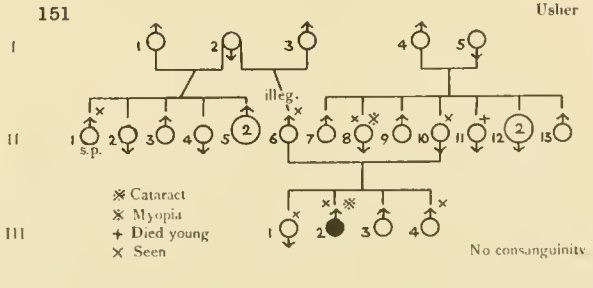
149 Usher



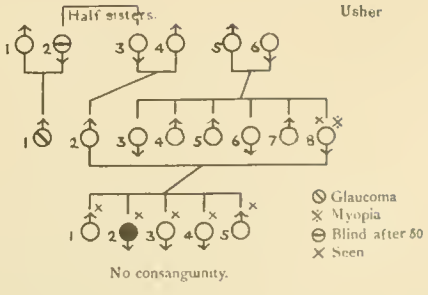
150 Usher



151 Usher



152 Usher



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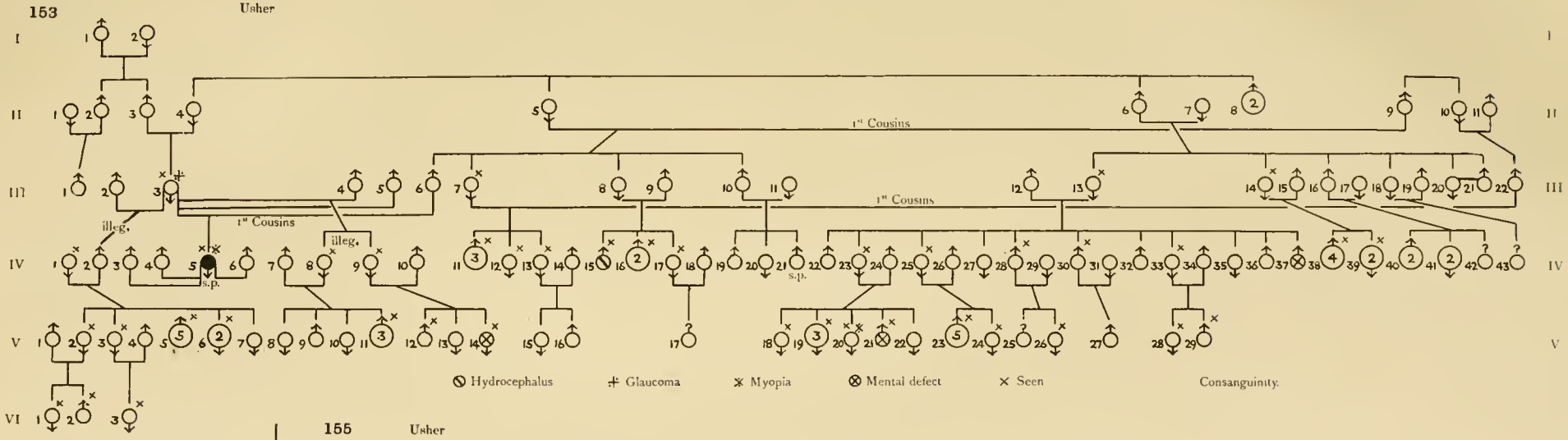
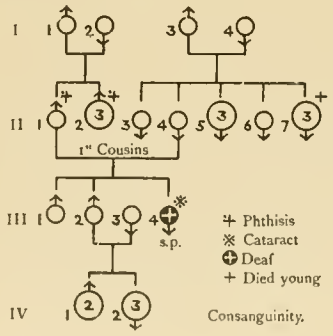
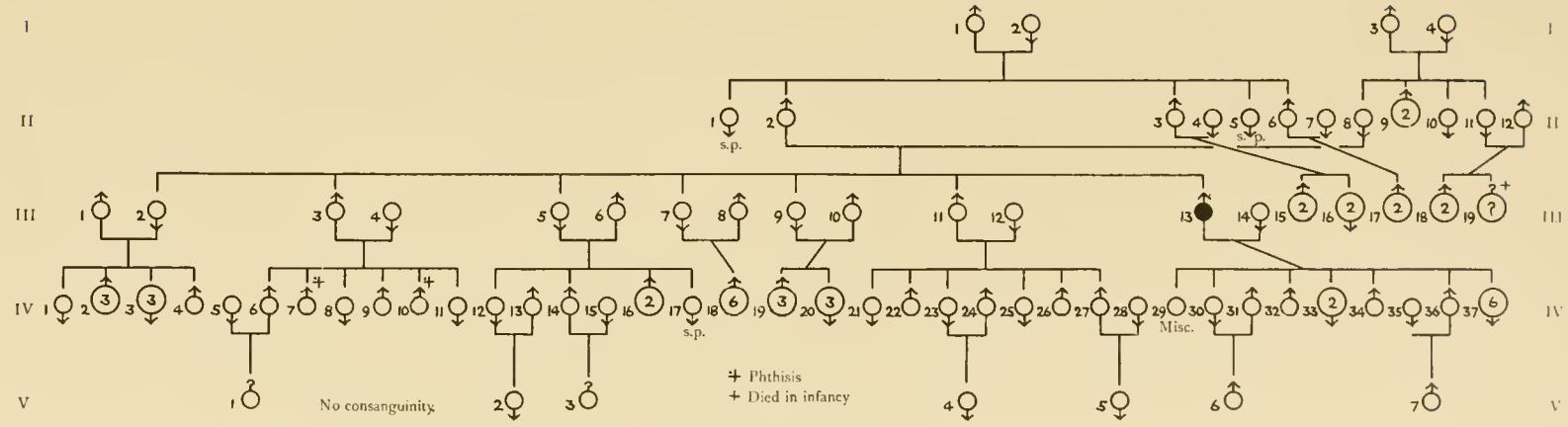
153 Usher



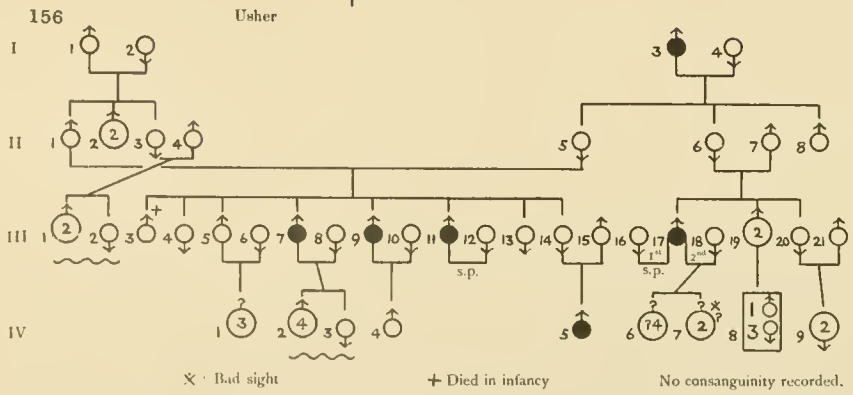
154 Usher



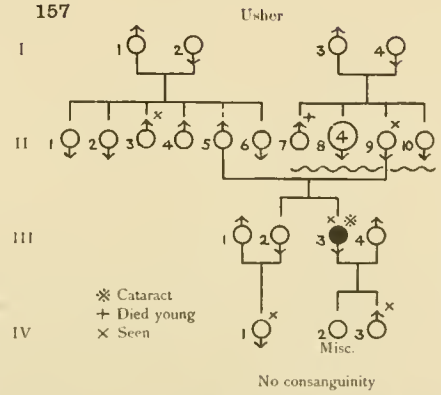
155 Usher



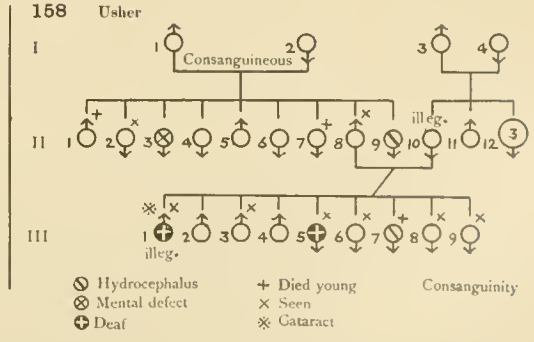
156 Usher



157 Usher



158 Usher



159 Usher

1st Cousins

2nd Cousins

illeg.

s.p.

※ Myopia
⊗ Mental defect
※ Cataract

⊕ Deaf
+ Died young
× Seen

Consanguinity.

160 Usher

illeg.

⊕ Deaf mutism
+ Died young
× Seen

No consanguinity.

161 Usher

Still-born

s.p.

illeg.

⊗ Mental defect
※ Cataract
⊕ Deaf
+ Died young
× Seen

No consanguinity.

162 Usher

1st Cousins once removed

※ Cataract
⊕ Deaf
× Seen
+ Raynaud's disease

Consanguinity.

163 Usher

+ Phthisis
⊗ Mental defect
※ Cataract
⊕ Deaf
× Seen

No consanguinity

164 Usher

1st H.

2nd H.

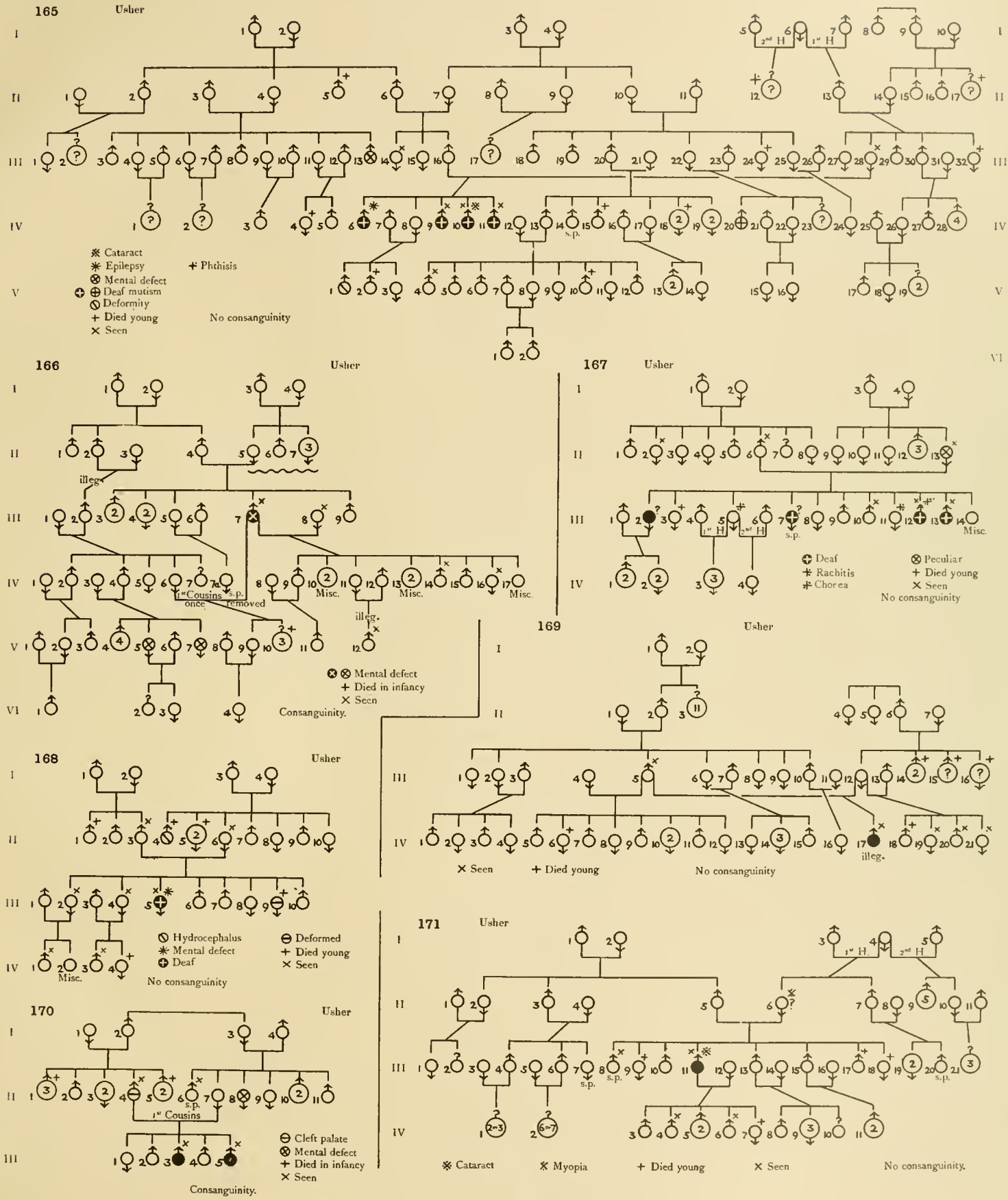
Misc.

Misc.

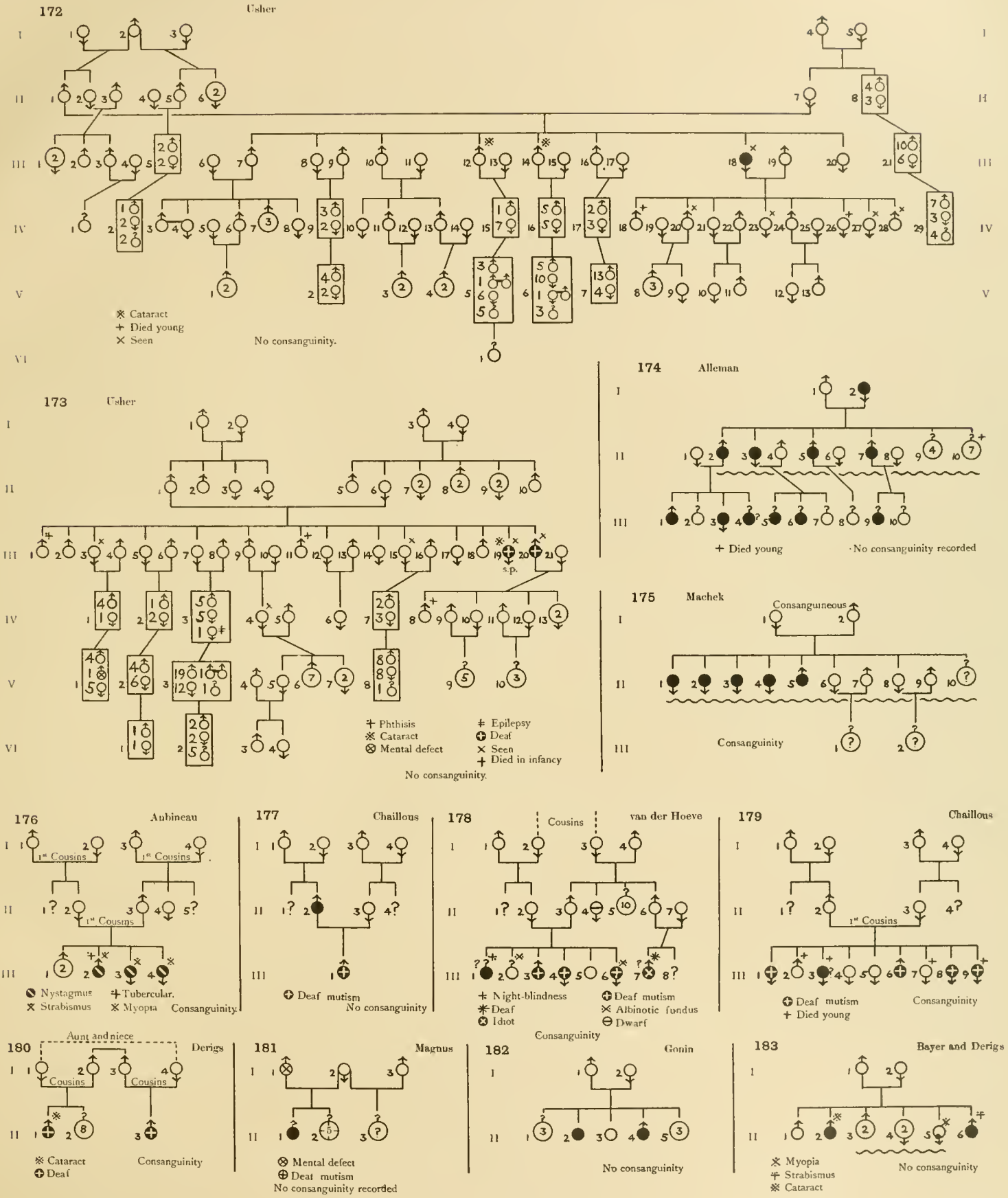
※ Myopia + Died young × Seen

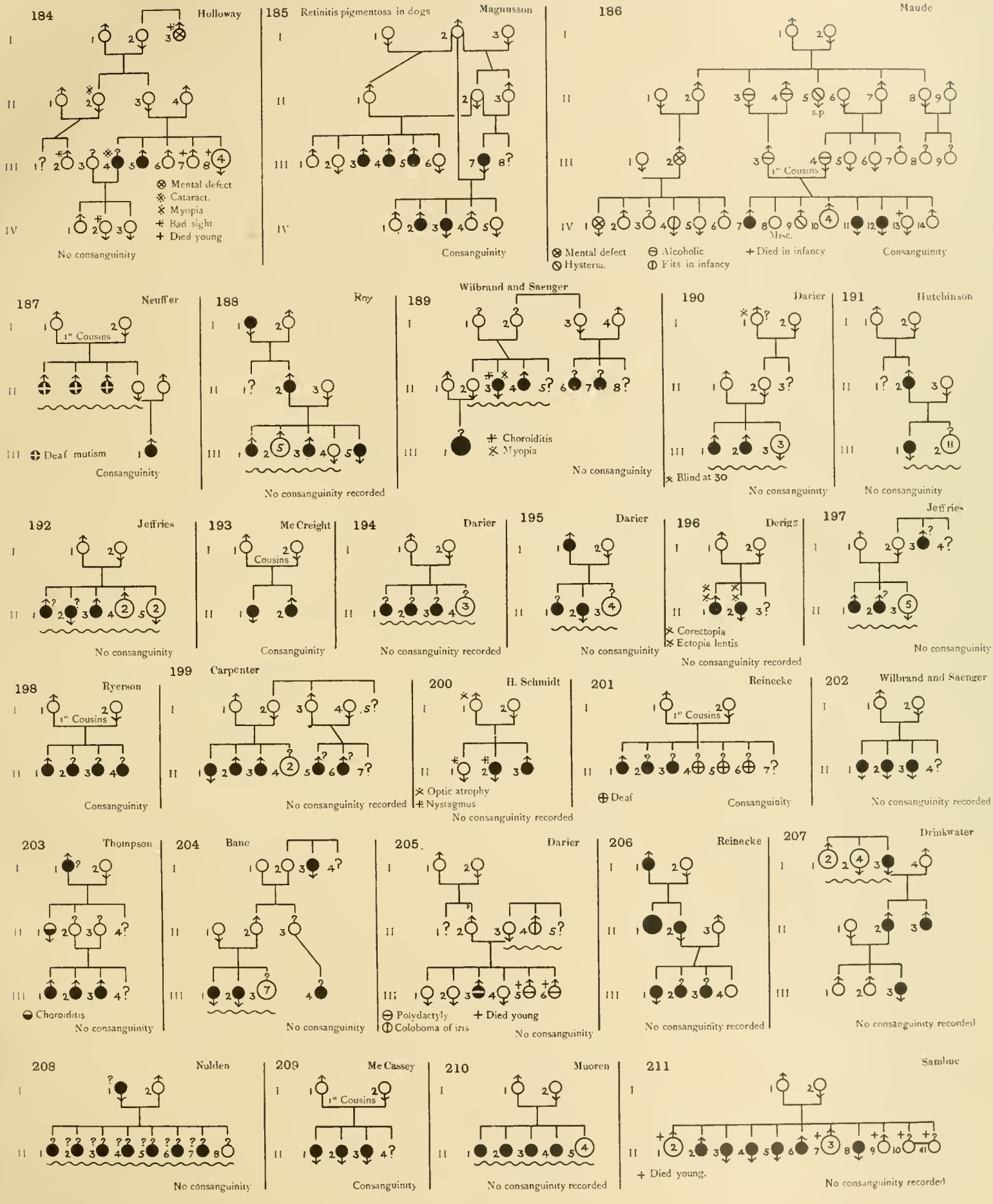
No consanguinity.

Issued by the Francis Galton Laboratory for National Eugenics.

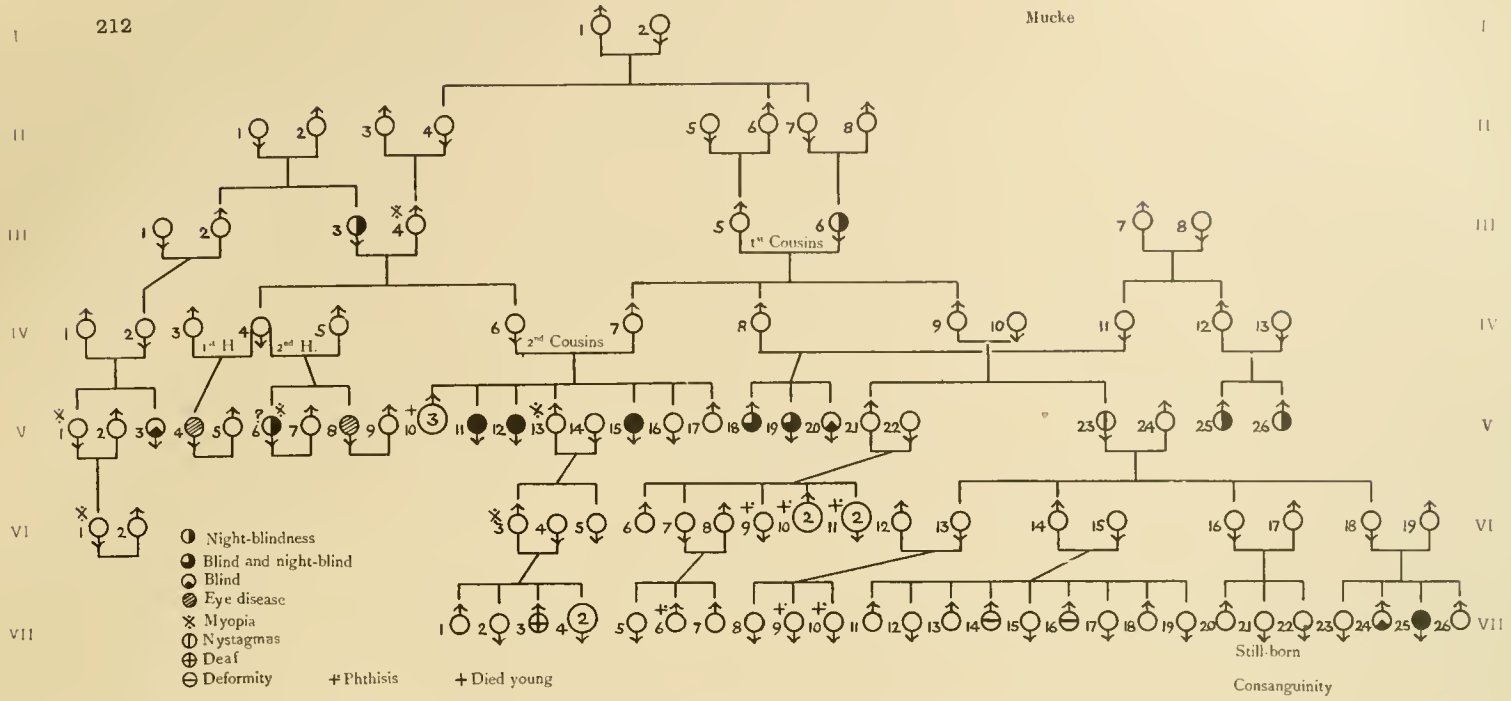


Issued by the Francis Galton Laboratory for National Eugenics.

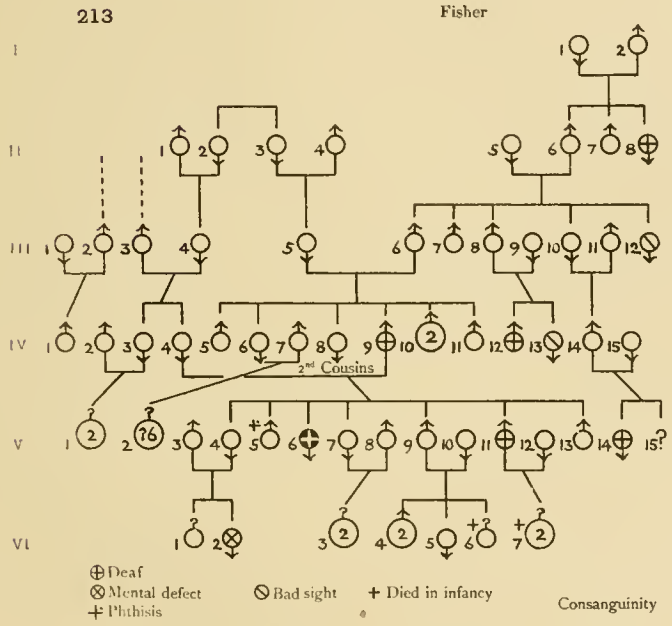

172 Usher
※ Cataract
+ Died young
× Seen
No consanguinity.
173 Usher
s.p.
+ Phthisis
※ Cataract
⊗ Mental defect
ǂ Epilepsy
⊕ Deaf
× Seen
+ Died in infancy
No consanguinity.
174 Alleman
+ Died young
No consanguinity recorded
175 Machek
Consanguineous
Consanguinity
176 Aubineau
1st Cousins
1st Cousins
1st Cousins
Nystagmus
Strabismus
Tubercular.
Myopia
Consanguinity
177 Chaillous
⊕ Deaf mutism
No consanguinity
178 Cousins
van der Hoeve
ǂ Night-blindness
✳ Deaf
⊗ Idiot
⊕ Deaf mutism
※ Albinotic fundus
⊖ Dwarf
Consanguinity
179 Chaillous
1st Cousins
⊕ Deaf mutism
+ Died young
Consanguinity
180 Aunt and niece
Derigs
Cousins
Cousins
※ Cataract
⊕ Deaf
Consanguinity
181 Magnus
⊗ Mental defect
⊕ Deaf mutism
No consanguinity recorded
182 Gonin
No consanguinity
183 Bayer and Derigs
※ Myopia
ǂ Strabismus
※ Cataract
No consanguinity


184 Holloway
⊗ Mental defect
※ Cataract.
✕ Myopia
+ Bad sight
+ Died young
No consanguinity
185 Retinitis pigmentosa in dogs Magnusson
Consanguinity
186 Maude
s.p.
1" Cousins
Misc.
⊗ Mental defect
⊖ Alcoholic
+ Died in infancy
⊘ Hysteria.
◐ Fits in infancy
Consanguinity
187 Neuffer
1" Cousins
Deaf mutism
Consanguinity
188 Roy
No consanguinity recorded
189 Wilbrand and Saenger
Choroiditis
Myopia
No consanguinity
190 Darier
Blind at 30
No consanguinity
191 Hutchinson
No consanguinity
192 Jeffries
No consanguinity
193 Mc Creight
Cousins
Consanguinity
194 Darier
No consanguinity recorded
195 Darier
No consanguinity
196 Derigs
Corectopia
Ectopia lentis
No consanguinity recorded
197 Jeffries
No consanguinity
198 Ryerson
1" Cousins
Consanguinity
199 Carpenter
No consanguinity recorded
200 H. Schmidt
Optic atrophy
Nystagmus
No consanguinity recorded
201 Reinecke
1" Cousins
Deaf
Consanguinity
202 Wilbrand and Saenger
No consanguinity recorded
203 Thompson
Choroiditis
No consanguinity
204 Bane
No consanguinity
205 Darier
Polydactyly
Coloboma of iris
+ Died young
No consanguinity
206 Reinecke
No consanguinity recorded
207 Drinkwater
No consanguinity recorded
208 Nulden
No consanguinity
209 Mc Cassey
1" Cousins
Consanguinity
210 Muoren
No consanguinity recorded
211 Sambuc
+ Died young.
No consanguinity recorded

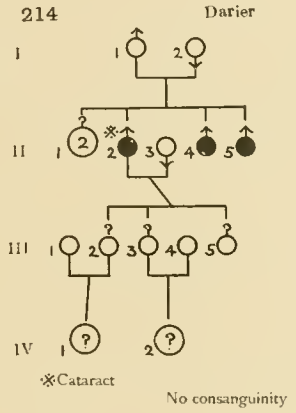
212 Mucke



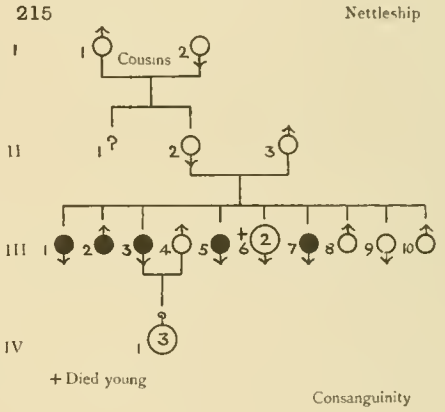
213 Fisher



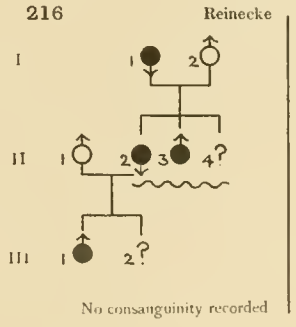
214 Darier



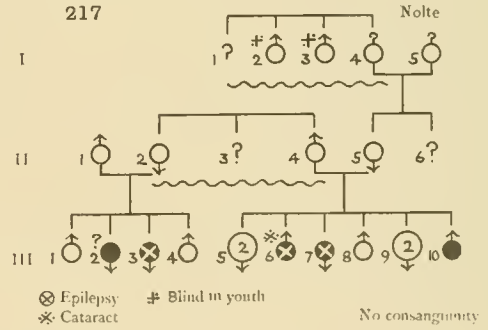
215 Nettleship



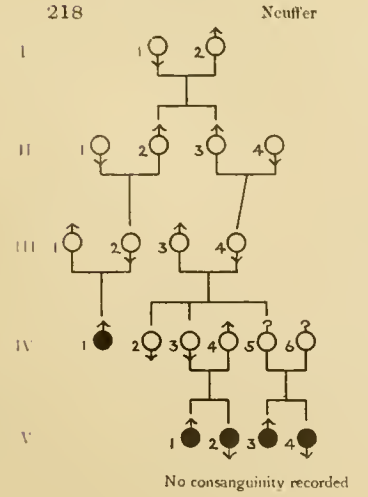
216 Reinecke



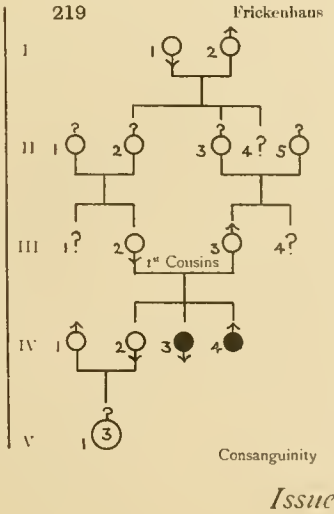
217 Nolte



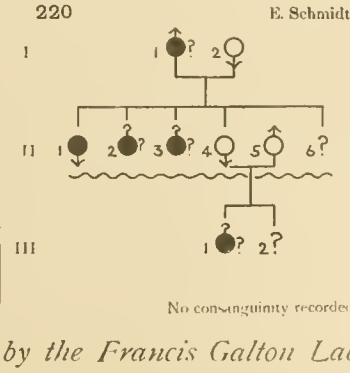
218 Neuffer



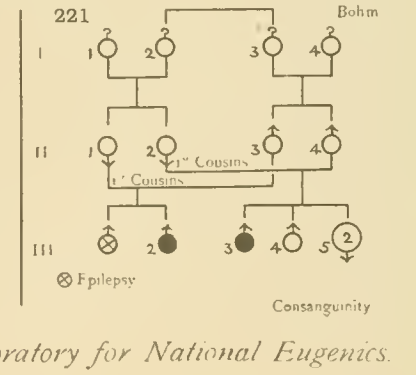
219 Frickenhaus

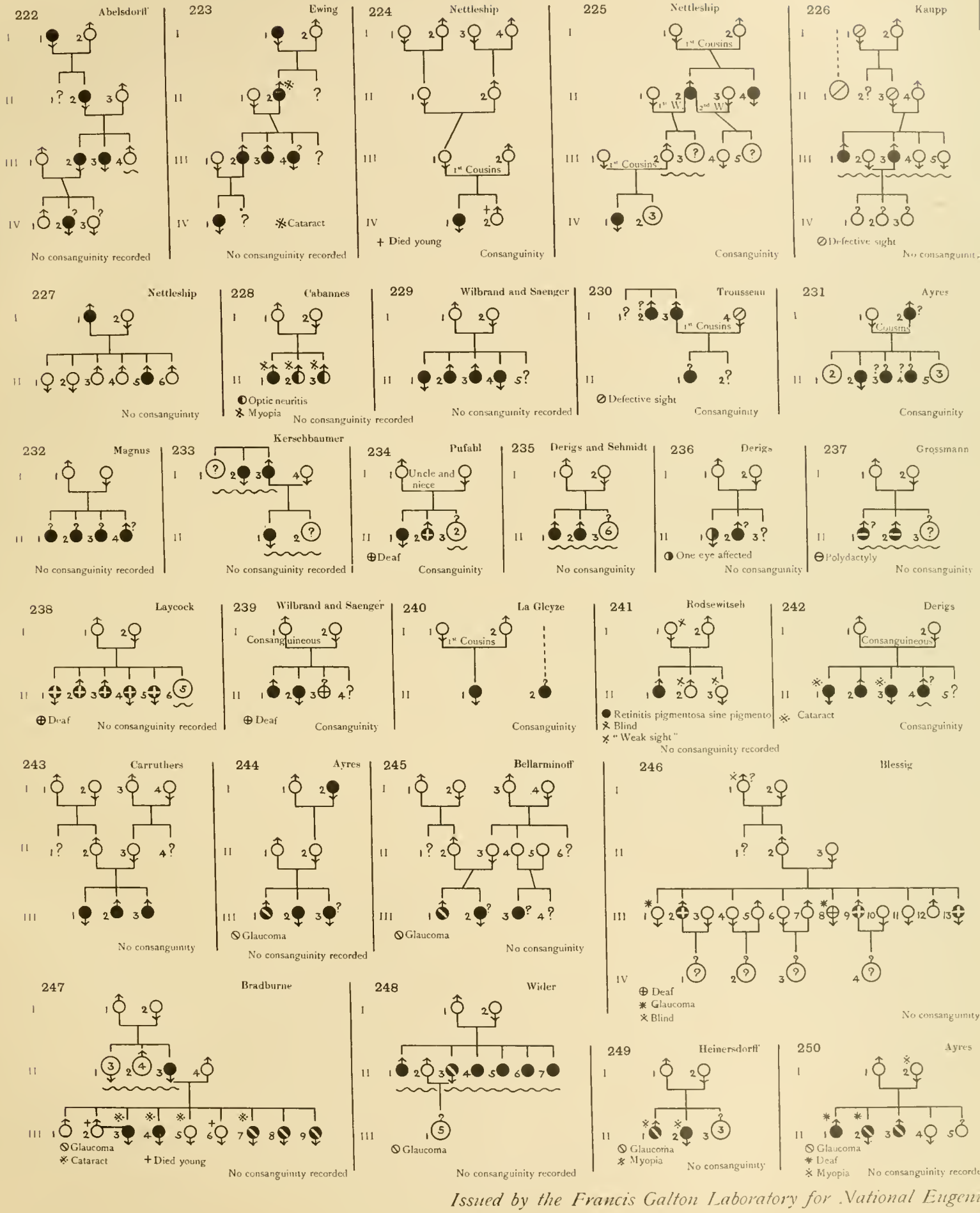


220 E. Schmidt

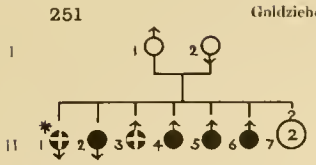


221 Bohm



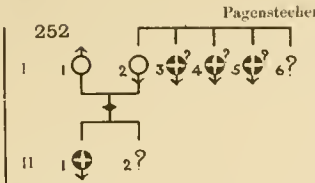

222 Abelsdorff
No consanguinity recorded
223 Ewing
Cataract
No consanguinity recorded
224 Nettleship
1st Cousins
+ Died young
Consanguinity
225 Nettleship
1st Cousins
1st W.
2nd W.
1st Cousins
Consanguinity
226 Kaupp
Defective sight
No consanguinit
227 Nettleship
No consanguinity
228 Cabannes
Optic neuritis
Myopia
No consanguinity recorded
229 Wilbrand and Saenger
No consanguinity recorded
230 Trousseau
1st Cousins
Defective sight
Consanguinity
231 Ayres
Cousins
Consanguinity
232 Magnus
No consanguinity recorded
233 Kerschbaumer
No consanguinity recorded
234 Pufahl
Uncle and niece
Deaf
Consanguinity
235 Derigs and Sehmidt
No consanguinity
236 Derigs
One eye affected
No consanguinity
237 Grossmann
Polydactyly
No consanguinity
238 Laycock
Deaf
No consanguinity recorded
239 Wilbrand and Saenger
Consanguineous
Deaf
Consanguinity
240 La Gleyze
1st Cousins
Consanguinity
241 Rodsewitsch
Retinitis pigmentosa sine pigmento
Blind
"Weak sight"
No consanguinity recorded
242 Derigs
Consanguineous
Cataract
Consanguinity
243 Carruthers
No consanguinity
244 Ayres
Glaucoma
No consanguinity recorded
245 Bellarminoff
Glaucoma
No consanguinity
246 Blessig
Deaf
Glaucoma
Blind
No consanguinity
247 Bradburne
Glaucoma
Cataract
Died young
No consanguinity recorded
248 Wilder
Glaucoma
No consanguinity recorded
249 Heinersdorff
Glaucoma
Myopia
No consanguinity
250 Ayres
Glaucoma
Deaf
Myopia
No consanguinity recorde

251 Goldzieher



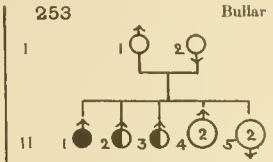
⊕ Deaf
✱ Glaucoma
No consanguinity

252 Pagenstecher



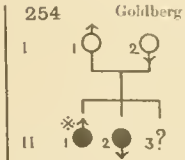
●? Chorio-Retinitis
⊕ Deaf
No consanguinity recorded

253 Bullar



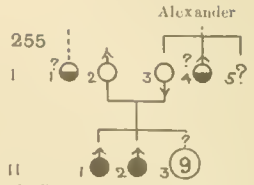
● Choroideremia
◐ Bad sight
No consanguinity

254 Goldberg



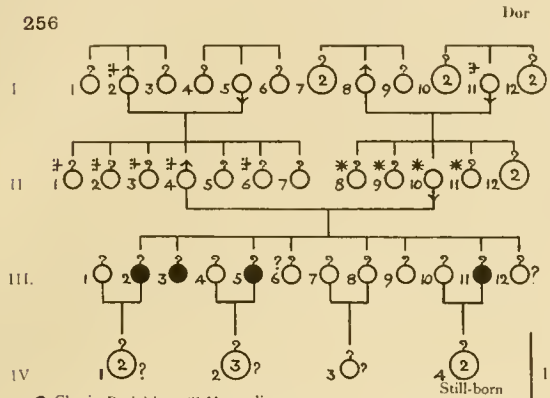
●? Choroideremia
※ Cataract

255 Alexander



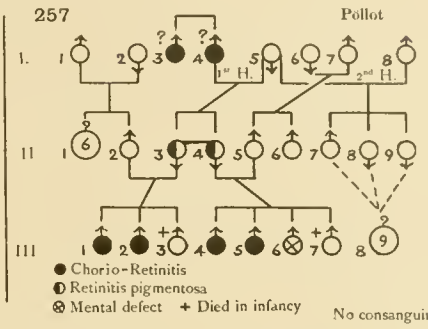
● Choroideremia
⊖ Night-blindness
No consanguinity

256 Dor



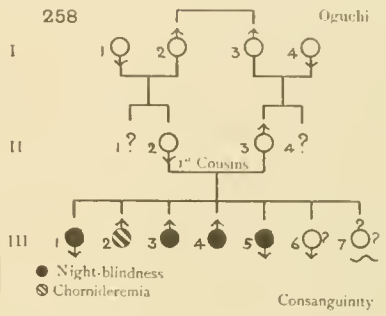
● Chorio-Retinitis ✱ Heart disease
ǂ Died suddenly
No consanguinity

257 Pollot



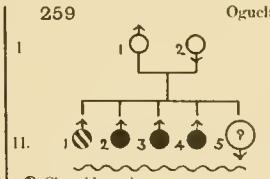
● Chorio-Retinitis
◐ Retinitis pigmentosa
⊗ Mental defect + Died in infancy
No consanguinity

258 Oguchi



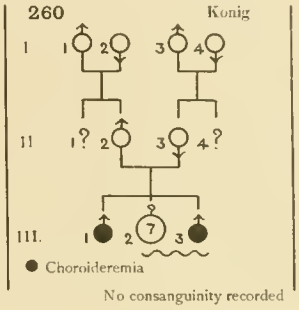
● Night-blindness
⊘ Choroideremia
Consanguinity

259 Oguchi



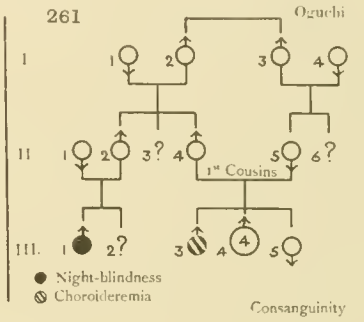
⊘ Choroideremia
● Night-blindness
No consanguinity

260 Konig



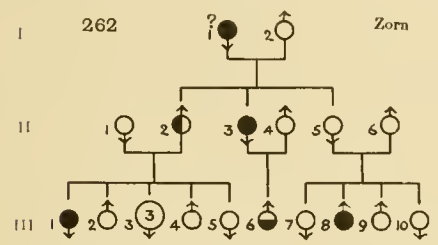
● Choroideremia
No consanguinity recorded

261 Oguchi



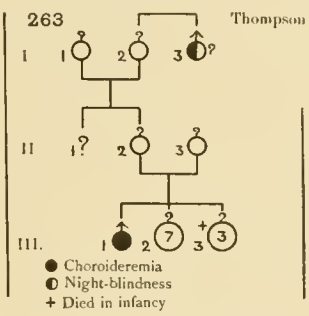
● Night-blindness
⊘ Choroideremia
Consanguinity

262 Zorn



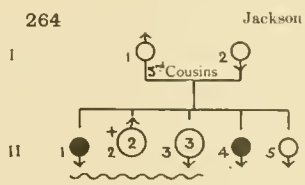
● Retinitis pigmentosa (atypical)
⊖? Atroph. gyr. ret et chor.
◐ Choroideremia
No consanguinity recorded

263 Thompson



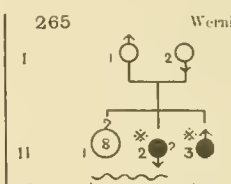
● Choroideremia
◐ Night-blindness
+ Died in infancy
No consanguinity

264 Jackson



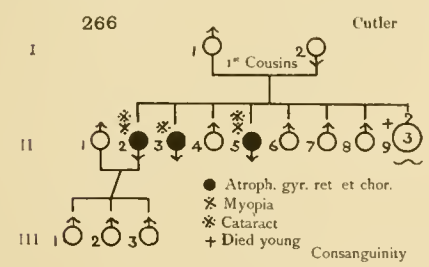
● Choroidal atrophy
+ Died young
Consanguinity

265 Wernicke



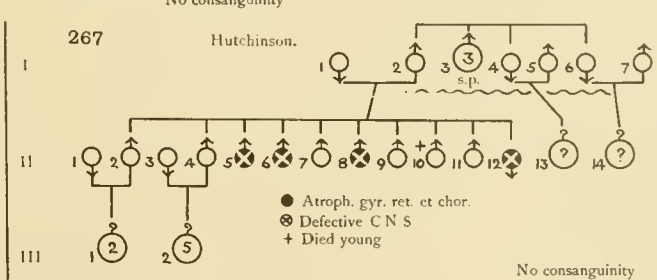
● Atroph. gyr. ret et chor
※ Cataract
No consanguinity

266 Cutler



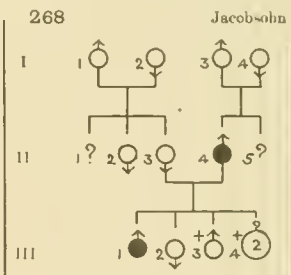
● Atroph. gyr. ret et chor.
※ Myopia
※ Cataract
+ Died young
Consanguinity

267 Hutchinson.



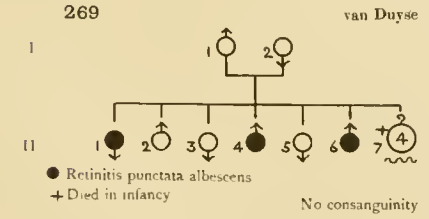
● Atroph. gyr. ret. et chor.
⊗ Defective C N S
+ Died young
No consanguinity

268 Jacobsohn



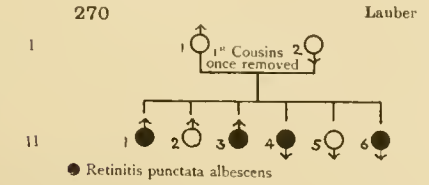
● Atroph. gyr. ret. et chor.
+ Died young
No consanguinity

269 van Duyse



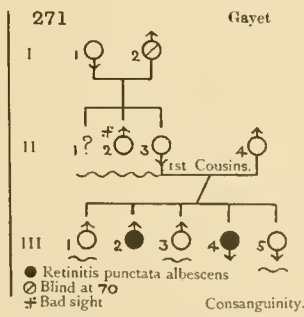
● Retinitis punctata albescens
+ Died in infancy
No consanguinity

270 Lauber



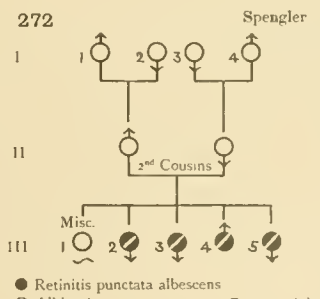
● Retinitis punctata albescens
Consanguinity

271 Gayet



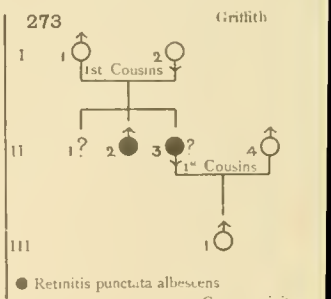
● Retinitis punctata albescens
⊘ Blind at 70
ǂ Bad sight
Consanguinity.

272 Spengler



● Retinitis punctata albescens
⊘ Albinotic
Consanguinity

273 Griffith



● Retinitis punctata albescens
Consanguinity

274 Nettleship

● Retinitis punctata albescens + Died young
⊖ Hare lip
Consanguinity

275 Nettleship and Collins

1st Cousins 1st Cousins 1st Cousins 1st Cousins once removed

● Retinitis punctata albescens
◐ Retinitis pigmentosa
+ Phthisis + Died young
Consanguinity

276 Nettleship

● Retinitis punctata albescens + Died young
+ Phthisis
No consanguinity

277 Ulrich

● Retinitis punctata albescens
◐ Retinitis pigmentosa
No consanguinity

278 Nettleship

1st W. 1st Cousins

● Retinitis punctata albescens
Consanguinity

279 Takaynsu

1st Cousins

● Retinitis punctata albescens
Consanguinity

280 Diem

● Retinitis punctata albescens
◐ Retinitis pigmentosa
⊗ Epilepsy
⊕ Deaf
No consanguinity

281 Healy and Drinkwater

● Retinitis punctata albescens
◐ Retinitis pigmentosa
No consanguinity recorded

282 Coben

● Retinitis punct. alb.
No consanguinity recorded

283 Wuestefeld

● Retinitis punct. alb.
◐ Retinitis pigmentosa
No consanguinity

284 Galezowski

1st Cousins

● Retinitis punct.alb.
Consanguinity

285 Cuperus

● Choroidal atrophy
✳ Myopia
⊘ Died Blind
No consanguinity

286 Lindner

1st Cousins

● ? Choroidal atrophy + Died in infancy
Consanguinity

287 Mauthner

● Choroideremna
⊘ Bad sight
No consanguinity recorded

288 Mouchot

● Retinitis pigmentosa + Died young
⊗ Idiot
+? Phthisis
No consanguinity

289 Merrill

● Retinitis pigmentosa
⊖ Coloboma of iris and choroid
No consanguinity recorded

290 Rampoldi

Consanguineous

● Retinitis Pigmentosa.
Consanguinity

291 La Serre

● Night-blindness
No consanguinity recorded

292 Ovelgun

● Retinitis Pigmentosa.
No consanguinity recorded

293 Mouchot

● Retinitis Pigmentosa.
+? Phthisis
No consanguinity

294 Mouchot

● Retinitis pigmentosa sine pigmento
⊕ Deaf mutism
No consanguinity.

GLIOMA RETINAE

295 Magnus

● Retinitis pigmentosa
No consanguinity

296 Pons

● Retinitis pigmentosa ✕ Corneal ectasia
+ Died in infancy No consanguinity

297 Richter

● Congenital night-blindness
+ Died in infancy No consanguinity recorded.

298 Flexner

No consanguinity recorded.

299 Marshall

+ Died in infancy
No consanguinity

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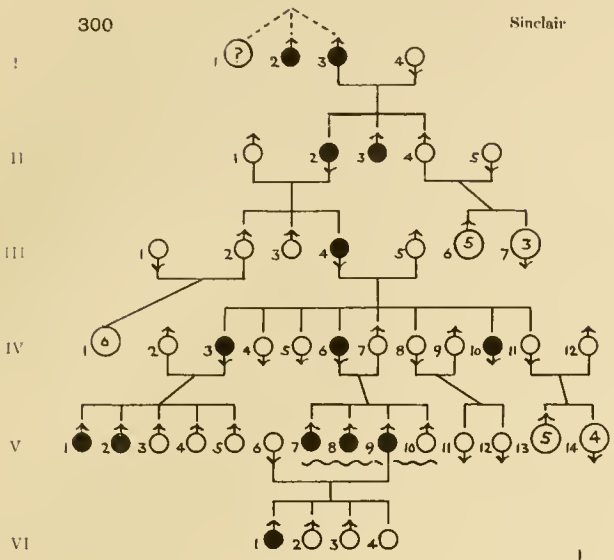
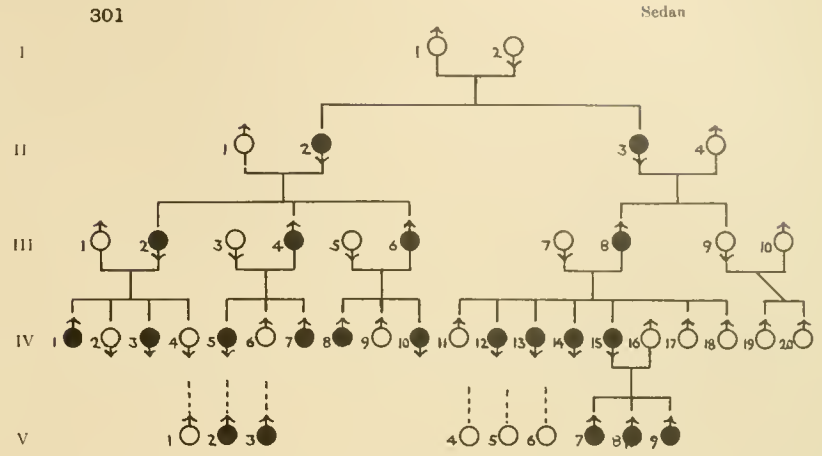
300 Sinclair



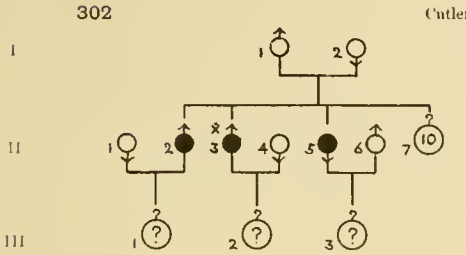
No consanguinity

301 Sedan



No consanguinity recorded

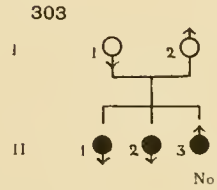
302 Cutler



✕ Nystagmus

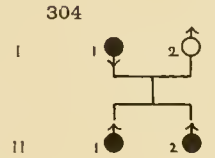
No consanguinity

303 Fuchs



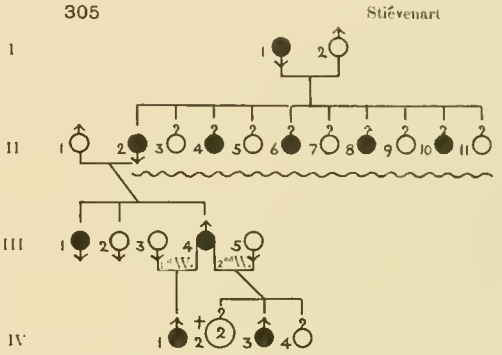
No consanguinity

304 Hudson



No consanguinity

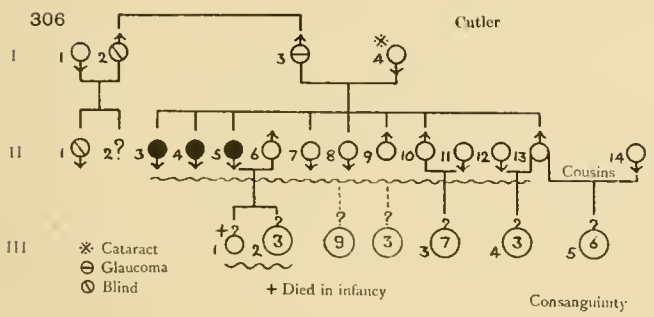
305 Stiévenart



+ Died in infancy

No consanguinity recorded

306 Cutler

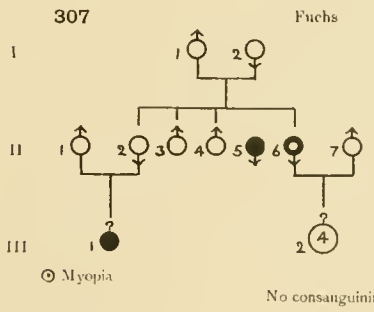


✕ Cataract
⊖ Glaucoma
⊘ Blind

+ Died in infancy

Consanguinity

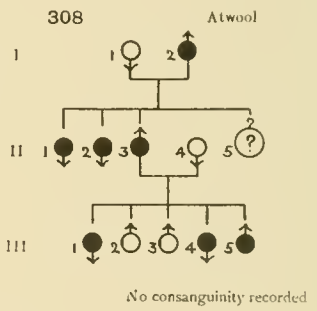
307 Fuchs



⊙ Myopia

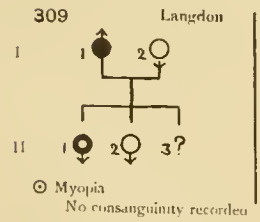
No consanguinity

308 Atwool



No consanguinity recorded

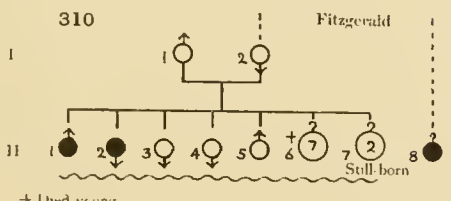
309 Langdon



⊙ Myopia

No consanguinity recorded

310 Fitzgerald

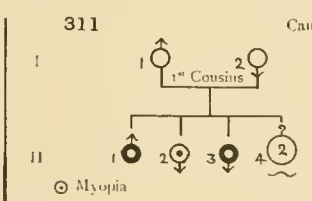


+ Died young

Still-born

No consanguinity

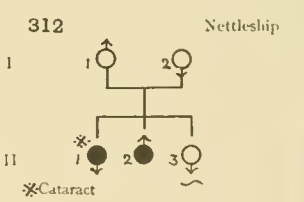
311 Cant



⊙ Myopia

Consanguinity

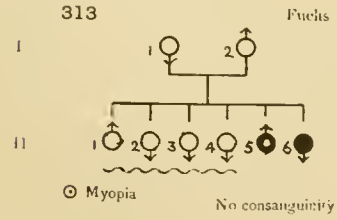
312 Nettleship



✕ Cataract

No consanguinity recorded

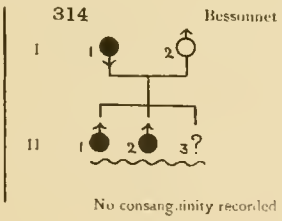
313 Fuchs



⊙ Myopia

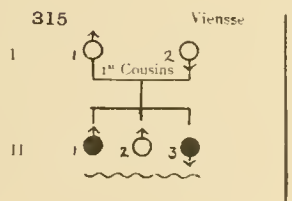
No consanguinity

314 Bessonnet



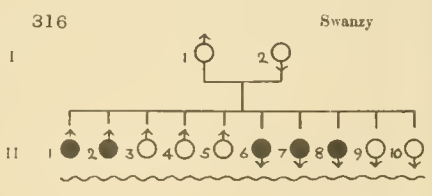
No consanguinity recorded

315 Viensse



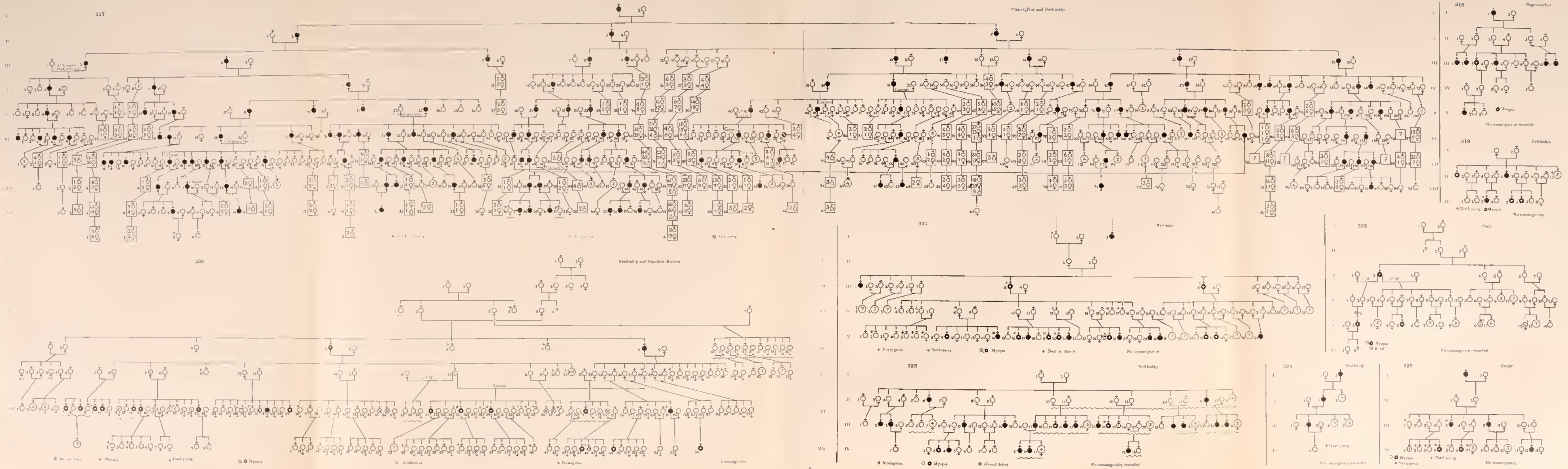
Consanguinity

316 Swanzy



No consanguinity

CONGENITAL STATIONARY NIGHTBLINDNESS



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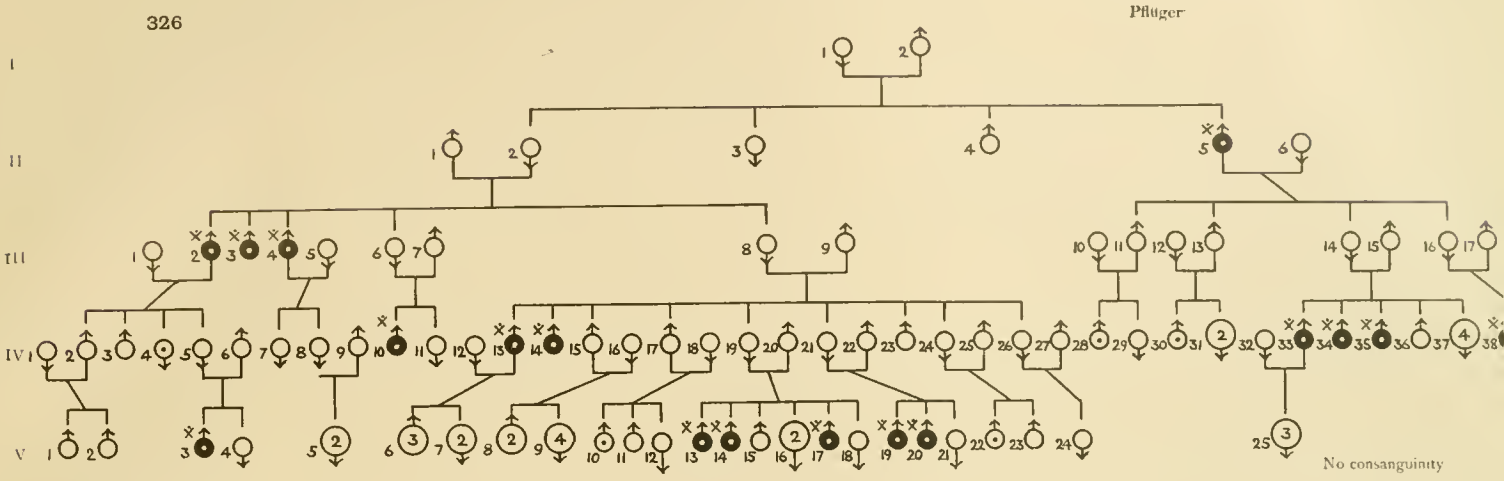
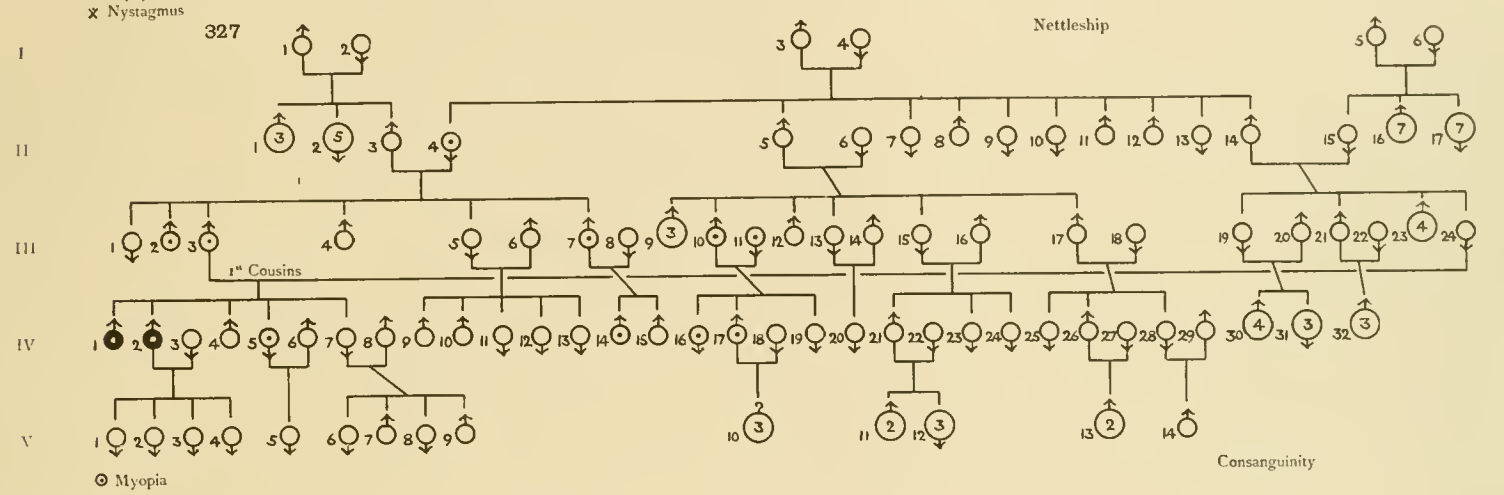
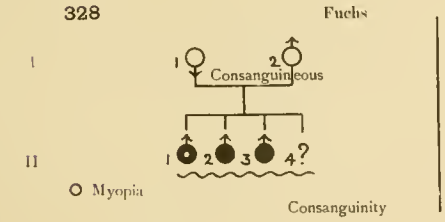
326 Pflüger



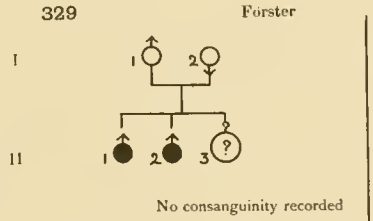
327 Nettleship



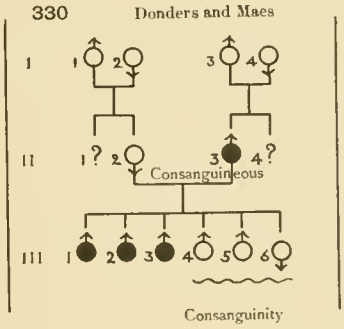
328 Fuchs



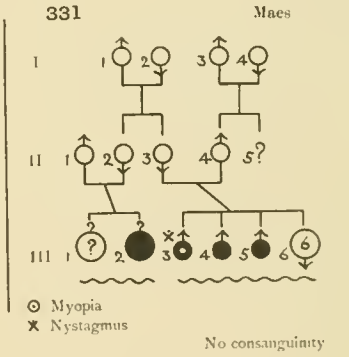
329 Förster



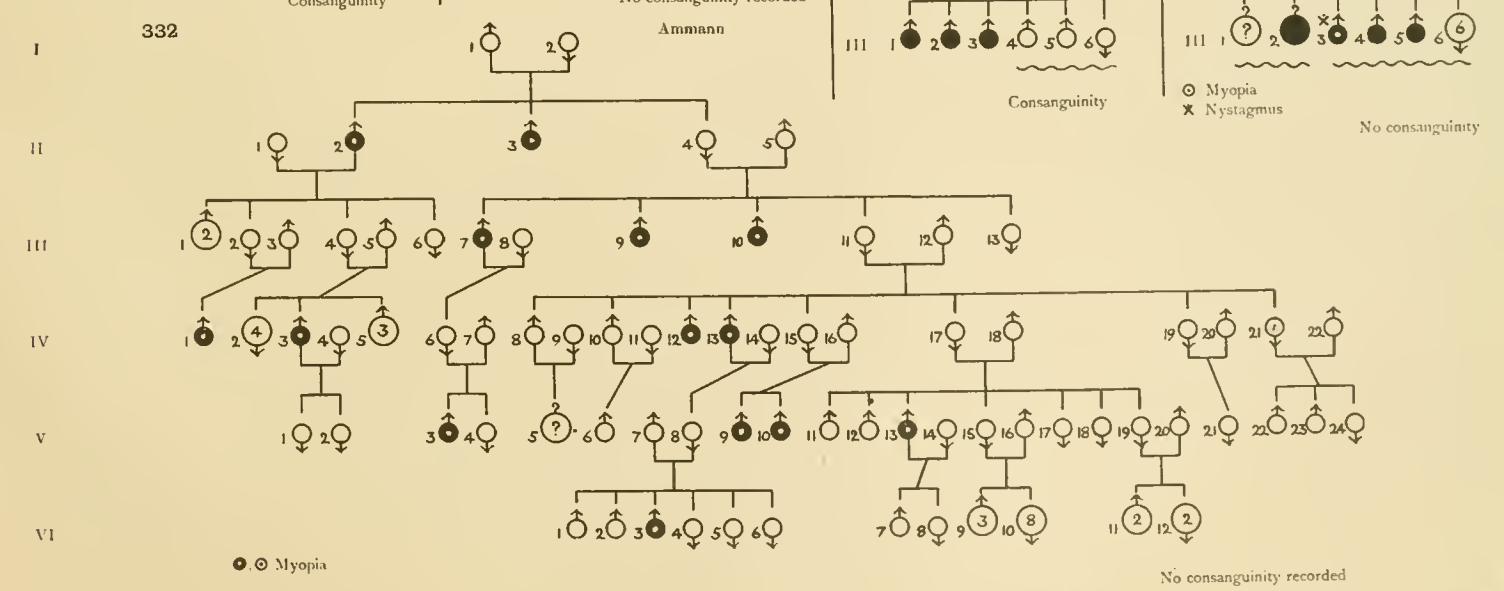
330 Donders and Maes

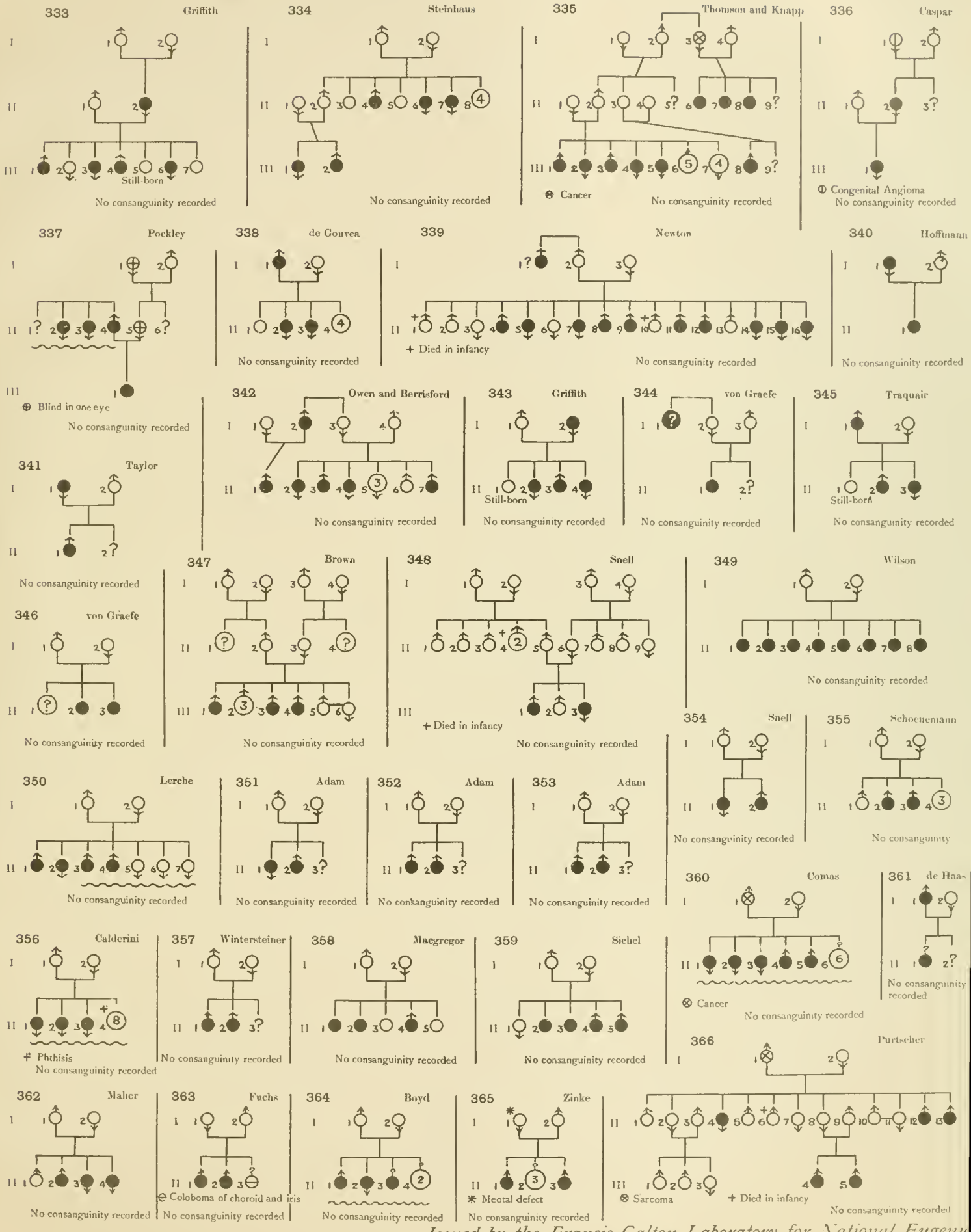


331 Maes



332 Ammann




333 Griffith
Still-born
No consanguinity recorded
334 Steinhaus
No consanguinity recorded
335 Thomson and Knapp
⊗ Cancer
No consanguinity recorded
336 Caspar
Ⓓ Congenital Angioma
No consanguinity recorded
337 Pockley
⊕ Blind in one eye
No consanguinity recorded
338 de Gouvea
No consanguinity recorded
339 Newton
+ Died in infancy
No consanguinity recorded
340 Hoffmann
No consanguinity recorded
341 Taylor
No consanguinity recorded
342 Owen and Berrisford
No consanguinity recorded
343 Griffith
Still-born
No consanguinity recorded
344 von Graefe
No consanguinity recorded
345 Traquair
Still-born
No consanguinity recorded
346 von Graefe
No consanguinity recorded
347 Brown
No consanguinity recorded
348 Snell
+ Died in infancy
No consanguinity recorded
349 Wilson
No consanguinity recorded
350 Lerche
No consanguinity recorded
351 Adam
No consanguinity recorded
352 Adam
No consanguinity recorded
353 Adam
No consanguinity recorded
354 Snell
No consanguinity recorded
355 Schoenemann
No consanguinity
356 Calderini
ǂ Phthisis
No consanguinity recorded
357 Wintersteiner
No consanguinity recorded
358 Macgregor
No consanguinity recorded
359 Siehel
No consanguinity recorded
360 Comas
⊗ Cancer
No consanguinity recorded
361 de Haas
No consanguinity recorded
362 Maher
No consanguinity recorded
363 Fuchs
e Coloboma of choroid and iris
No consanguinity recorded
364 Boyd
No consanguinity recorded
365 Zinke
✱ Meotal defect
No consanguinity recorded
366 Purtscher
⊗ Sarcoma
+ Died in infancy
No consanguinity recorded

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